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PHARMACOLOGY

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PHARMACOLOGY

ACTION AND USES OF DRUGS

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PREFACE.

As a teacher of Pharmacology, the author was frequently asked by his pupils for a small and concise text-book which would give the facts essential to an elementary medical student without extensive discussions of opposite opinions.

It has been in an attempt to supply such a work that the following pages have been written. Although the volume is small, all the standard literature was consulted and carefully weighed before being admitted or rejected, and the criterion was always to preserve all the essential, known facts regarding the action of drugs, but to reject vague and contradictory statements of no importance which would but confuse the beginner.

At the end of each group description there is a brief summary of the general action; following the latter is a short statement concerning the uses and applications, and, lastly there is a concise description of the different preparations used in medicine with their doses.

The author does not claim for the book that it is an exhaustive treatise on Pharmacology suitable for advanced students of the subject, but that it may be found useful to the ordinary medical students and also to the general practitioners who may use it to review their medical school instruction. As one of the leading pharmaceutical journals suggested in writing a criticism on the first edition, this volume might also be serviceable to pharmaceutical students for the study of drug action.

In this second edition the author has attempted to incorporate all new facts in pharmacology or in pharmaco-therapy which have been developed since the previous edition. Some minor changes in group arrangement have also been made.

In conclusion, the author wishes to reiterate his thanks to the

hundreds of workers in pharmacology whose original monographs and text-books he has consulted.

The author is also very grateful to the pharmacologists, students, and others for the kind manner in which they received the first edition, and also for valuable criticisms which some kindly offered.

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INTRODUCTION.

The treatment of disease is as much an inherent part of the nature of human beings and of the instinct of self-preservation as the taking of nourishment. We see evidence of dietetic, physical and also drug therapy even in the lower animals. It is a well-known fact that household animals refrain from eating much, or indigestible articles when suffering from stomach upsets. Cats and dogs when suffering from some gastro-intestinal disturbance go into the fields to find grasses with emetic or purgative properties. Men in uncivilized conditions all have some sort of crude medical knowledge and, like the American Indians, often have some "medicine man." The white race has had ups and downs in the status of medical knowledge. Recent discoveries seem to show that the ancient Egyptians, even thousands of years ago, had probably as fully a developed medical system as we have, with as many if not more specialties. There followed a curve of decadence which probably reached its lowest period shortly after the fall of the Roman Empire. After this the curve then rose again with the work of the Arab physicians, followed by that of the Christians, until it has again in our days reached a high position.

We have but little evidence left us of what was the knowledge of drugs of the ancients at the time of their maximum medical development, but we do know positively that since the first centuries of the Christian era, our knowledge has more or less steadily increased.

One great drawback, still existing, which has hindered our progress in the knowledge of diseases and their treatment, has been shiftless observations and the drawing of unwarranted conclusions. Thus, with some drugs every conceivable action and curative value has been described by some and contradicted by others.

At the beginning of the last century, the great French physiologist, Magendie, introduced a new and more accurate method of studying drugs by applying them to animals where all conditions were checked. After him, Claude Bernard and a host of others followed this new subject of experimental study of drugs, which gave us very valuable information as to many hitherto unknown properties of old remedial agents and led to the discovery of new ones. Thus, by the experimental method used both on animals and man, there have developed all the modern methods of anæsthesia, of antisepsis, of treatment by antitoxines and vaccines and the coming field of Therapia sterilisata magna, just begun by Ehrlich in the substance salvarsan.

It, however, had become the tendency to draw too generalized conclusions from the study of the action of remedial agents on certain species of animals in health and to attribute them theoretically to other classes of animals and to diseased conditions. This not infrequently led to fallacious results, for although many drugs present the same general type of action in various species of animals, nevertheless, there are a vast number which present radical differences of action. This difference of action also exists in the same species under pathological conditions or when other drugs are used at the same time.

In this way it has been shown that epinephrin, which usually constricts powerfully the blood vessels in mucous membranes, entirely fails to do so if there is any inflammatory reaction present. The difference between the action of antipyretics in health and disease was shown years ago. They decrease febrile temperature and have no effect on normal temperature. It has been found that starvation has a marked effect upon the action of drugs. With some, their action is increased, while with others, it is much diminished. Formerly, caffeine was almost always given with acetanilid and other coal tars, with the idea of counteracting the depressant effect of the latter by the stimulant effect of the former on the heart and respiration. Experimentally, it was shown that caffeine not only did not diminish the noxious effect of some coal tars but increased them.

From what has been said, it is plain that we cannot draw too generalized conclusions from experimental work, and that in applying drugs in practical medicine, we must bear in mind the innumerable conditions which may affect the action of our agents. Thus, we still are in the infancy of our knowledge of drugs and other therapeutic agents, and we must always remain open to changes in our views when new works demolish the old theories.

The statements which follow are, to a certain degree, dogmatic in order to give something definite for the beginner to start with; nevertheless, they should not be regarded as immutable laws.

Therapeutics *is that subject which treats of the methods used in curing or alleviating disease.* These may be divided into four groups; first, dietetic, including qualitative and quantitative changes in the diet; second, physical and physicochemical, including the application of electricity, massage, heat and cold; third, suggestive, such as hypnosis; and fourth, medicinal. This volume is devoted to the consideration of medicinal agents or drugs.

A **drug** *is any substance other than a food stuff or a mechanical agent, which produces changes in a living organism.*

These changes, constituting the **action,** may be beneficial or harmful depending upon the quantity of the drug used and upon the conditions of the organism receiving it. When a drug is used in suitable doses to produce beneficial influences, it is said to be a **medicine.** When it is used in such doses as to produce harmful effects, it is said to be a **poison;** e. g., chloral in small doses is a valuable medicine to produce sleep, while in larger quantities it is a powerful narcotic poison.

Drugs produce their action in a living organism either by increasing, decreasing or stopping one or more functions, or in infectious diseases, by destroying the parasites or the effect of their noxious products.

When employed in medicine for the treatment of disease, they are used according to these principles.

Thus for too high temperature, we employ antipyretics to reduce it; for excessive secretion of hydrochloric acid and increased tonic contraction and spasm of the pylorus, we give atro-

pine, which decreases both. When the heart is abnormally weak, we give digitalis to increase its strength, and when the kidneys are not excreting a sufficient amount of urine, we stimulate them with some of the various diuretics. As examples showing therapy directed against the specific cause of disease, we have the use of quinine in malaria, mercury and salvarsan in syphilis, diphtheria antitoxine in diphtheria, vermicides for intestinal parasites, etc.

The science which deals with the study of the action of drugs is called **Pharmacology** *or Pharmacodynamics.* More recently, that term has been reserved particularly for the subject which treats of the action of drugs on normal animals. *For the scientific study of drugs upon diseased organism, the name* **experimental therapeutics** is now more commonly used. If we consider drugs as poisons and study the symptoms which they produce in both accidental and intended cases of poisoning and also the methods used for their detection, the subject is known as **Toxicology,** and is in part included in pharmacology.

The action or changes produced in a living organism by drugs, may be either of a chemical or of a physicochemical nature. Most drugs unite chemically with some constituents of the organism, and, by virtue of this union, change its functions. Some, such as the neutral salts, act in part through their physical relations to the tissues.

A drug may produce alterations in the functions of a part to which it is applied before it has entered the blood circulation. These changes may consist of loss of sensation, inflammation, with its symptoms, necrosis and astringent effect, and constitute **local action.** The changes produced by a drug after it has been absorbed into the circulation, are known as **general action.** Thus after a subcutaneous injection of morphine, its local action is irritation at the place of application, while its general action, is the production of sleep.

Intensity of action *depends upon many factors besides the quality of the drug and the quantity given. It is dependent also upon differences in the condition of the subject receiving the same, such as its species, race, sex, age, habits, weight, states of nutrition*

and of health and individual susceptibility. A man is much more susceptible to morphine than a dog, likewise one species of frogs differs from another in this respect. Very young children, old persons and females, are more easily affected by medicinal agents than vigorous males. As a rule, the heavier the subject, the greater is the quantity of a drug which is required to produce a certain effect. With some drugs, such as morphine, cocaine and alcohol, habituation is a most potent factor in affecting the intensity of action, e. g., occasionally morphine or cocaine habitués may take without any apparent immediate effects several times the ordinary fatal dose of these poisons. Some individuals show very intense or peculiar symptoms with a quantity of a drug which would not produce these in most persons. This susceptibility is known as **idiosyncrasy.**

The **intensity of action** *of a drug depends to a certain extent upon its concentration in the blood. The concentration in turn depends upon the difference between the rate of absorption and excretion.* Hence, the more rapid the absorption and the slower the excretion, the greater is the concentration when other conditions are equal. The reverse is also true. Such an active drug as curare, the Indian arrow poison, produces no effect whatever when given by the mouth, because it is so slowly absorbed by the gastro-intestinal tract, and so rapidly excreted by the kidneys, that there is never a sufficient concentration in the blood to cause any action. When either excretion is stopped by tying the renal arteries, or when the absorption is made more rapid by giving this drug under the skin, or into the blood vessels, it causes severe symptoms.

The rate of **absorption** *depends to a certain extent upon the physical characters of the drug, such as volatility, diffusibility and solubility in water, and it is promoted by all these factors. Of importance on the part of the organism is the place of application and the efficiency of the circulation. Thus drugs are most rapidly absorbed from serous surfaces such as those of pleura and peritoneum. The next most efficient absorbing surfaces are the subcutaneous tissues. Drugs are most slowly absorbed from the mucous membranes of the gastro-intestinal tract.* A good blood circulation is essential to

good absorption, for, in heart diseases when the circulation is very inadequate and œdema is present, a drug may not be absorbed easily from serous membranes or subcutaneous tissues.

Excretion, *like absorption, is usually more rapid with volatile and diffusible substances and with those soluble in water.* The rule is not absolute, for even though the salts of the sodium sulphate group and also some sapotoxins are soluble in water, yet they are absorbed with difficulty, and on the other hand, many metals, as copper, lead and iron, even when taken in the form of very soluble salts, form compounds with the proteids of the tissues which are tenaciously retained by the organism, making excretion very difficult. This all tends to show that the specific chemical nature and affinity of drugs is of very great importance in relation to absorption, excretion and action.

Drugs are excreted either unchanged, or after chemical combination with some products of the organism, or after oxidation to simpler compounds. For example, ether is excreted unchanged, chloral is in part combined with glycuronic acid, and is excreted as urochloralic acid. Alcohol is in most part oxidized to, and excreted as, carbon dioxide and water.

Excretion may take place through the kidneys, intestines, stomach, liver, salivary glands, lungs, skin, etc. Most drugs have a selective preference for one channel or another, e. g., morphine is excreted almost exclusively by the stomach and intestines, while strychnine is excreted by the kidneys, and ether by the lungs.

Subordinate to the study of the action of drugs, is the study of their physical and chemical properties. The division treating of these is known as **Materia Medica.** It includes the subjects of Pharmacy, or the art of compounding drugs, that of Pharmacognosy, or the study of the methods used in the recognition of drugs, that of Posology, or the study of doses, and lastly, the study of prescription writing.

A large percentage, but not all drugs are described in an official book called "*Pharmacopeia*" in most countries and "Codex" in France. These "Pharmacopeias" of different countries differ

from each other considerably in the choice of drugs and preparations and also in the strength of these. During the past few years, greater efforts have been made to reach greater unity.

In the following pages our attention will be occupied mainly with the action and uses of drugs. There will also be given a very brief notice of the physical and chemical characteristics and doses.

The drugs are divided into groups, which are composed of members having the same or nearly the same general pharmacological action. The first group consists of drugs whose characteristic action is a depression of the brain.

PHARMACOLOGY.

PART I.

GROUP OF ETHER AND CHLORAL.

This group contains a series of drugs whose chief action is the production of **narcosis.** It includes most of the fluid and volatile hydrocarbons, alcohols, ethers, neutral esters, aldehydes and ketones of the aliphatic series; also, their halogen derivatives.

The physical properties of the members of this group influence to a considerable degree their intensity of action. As a rule, the more volatile are the most active while the solid nonvolatile, which are insoluble in water, are the least active. Thus of the hydrocarbons, the very volatile pental is very active while the nonvolatile and insoluble paraffine is absolutely inert.

The very volatile compounds are absorbed by the lungs in the form of vapors in sufficient quantities to produce complete paralysis of the brain. Their intensity of action can be easily regulated when administered by these channels while very intense depression of the brain for a short time can be produced. Thus the very volatile compounds are ideally suited to produce unconsciousness during surgical operations and are called **anæsthetics.** The solid nonvolatile members are more appropriately administered by the gastro-intestinal tract, and their absorption and excretion are slower; therefore their effects come on more slowly and less intensely but last a longer time. They are more suitable when we wish to produce a mild depression of the cerebrum to induce sleep, and are called **hypnotics** or soporifics.

The anæsthetics and hypnotics do not differ markedly from each other in their quality of action, but only in their clinical application on account of their difference in physical properties. Small quantities of the anæsthetics may produce simple sleep, while large doses of hypnotics may give rise to complete unconsciousness or anæsthesia. The sleep produced by the former is of too short duration to be of practical use, while the anæsthesia produced by the latter cannot be properly regulated.

The question as to **how narcotics produce their effect** has been one of the most discussed in the field of pharmacology. Wild theories have been advanced in the past, such as, that narcosis is due to vagus inhibition; or to changes in the blood preventing the latter from nourishing the brain, or to semi-coagulation of nerve cells. More recently the theory of solubility and affinity of lipoid substances of the brain cells towards narcotics has been advanced by Myer and Overton and has held ground among many pharmacologists for the last ten years. It presupposes that narcotics produce their action varying in intensity according to their power of dissolving fat-like substances, and therefore the lecithin and cholestin from the nerve cells, and that this suspends the activity of the latter. This theory is not unattackable, since there are many substances, especially benzol derivatives, whose affinity for fats is greater than for water, and yet which do not produce narcosis.

It is probably true that the greater solubility in fatty substances than in water, aids the penetration of the narcotics into the nerve cells, but the action is probably due to specific combination of the narcotic with some essential molecule of the cell whose function is suspended when this happens. In support of such a combination it has been found that the amount of chloroform present in an anæsthetized animal was much greater in the brain than in certain of the tissues, as the muscles, etc. The firmness of the combination of anæsthetic with brain tissue depends upon the partial pressure of the drug. When the amount of an anæsthetic is decreased in the blood by allowing free respiration without the introduction of more of the narcotic, the combination breaks up in

the nerve cells affected, the cells regain their functional activity and the individual regains consciousness.

The action of most narcotics on the **central nervous system** consists of a successive *depression of the cerebrum, spinal cord, and lastly, of the medulla.* The first effect on the cerebrum is a decrease in the sensibility to external stimuli not of a painful character, also, a dulling of the intellect and a decrease in voluntary movements. On account of the lowering of judgment and of other higher psychical functions, great talkativeness and excitement may be observed, especially when the surroundings and mental conditions of the subject are appropriate. Then, follows complete paralysis of the cerebrum with unconsciousness and loss of the sensation of pain, also, paralysis of the cord with abolition of reflexes, and muscular relaxation. At last the medulla is paralyzed, and there is stoppage of respiration and fall of blood pressure, due to the depression of the respiratory and vasomotor centres. The stage in which complete unconsciousness is present and muscular movements are suspended, is that called surgical anæsthesia. The last one, with paralysis of the medulla, is the fatal stage.

The **vasomotors** supplying the smaller vessels of the skin and surface of the brain are paralyzed at the beginning of the action of the narcotics. The reddening of the face and body observed after a few glasses of wine, is also present at the beginning of anæsthesia with ether or chloroform. Because of the decrease of muscular movements, the production of heat is diminished, but on account of the dilatation of the superficial blood vessels, the loss of the bodily heat is increased and the **temperature** of the organism may be lowered several degrees. During prolonged surgical anæsthesia, if the patient is not properly protected, the loss of heat may be sufficient to increase the collapse from other causes.

ETHER or Ethyl Ether which is easily volatilized is a typical anæsthetic. It was the first discovered and has been, to the present time, the most extensively used in this country. Its typical action may be seen after direct introduction into the blood streams

or after administration through any one of the channels of absorption, as the subcutaneous tissues, gastro-intestinal tract, rectum and lungs. The latter channel has been found to be preferable because the absorption and excretion can be more easily regulated and the irritation is less than by most of the others.

Except for a very small amount which passes out by the kidneys, ether is almost entirely *excreted by the lungs*. The small percentage excreted by the kidneys produces at times marked irritation of these organs. After prolonged etherization, besides evidences of *renal irritation*, the urine may contain glycuronic acid, glucose, acetone and diacetic acid. These are probably the result of a disturbance in the metabolism.

Since the most appropriate channel for the administration of ether is the lungs, the study of the conditions influencing its absorption through these organs is of great importance.

Its **absorption and excretion by the lungs** are subject to the physical laws of partial tension of gases. The walls of the alveoli of the lungs act as a permeable membrane between the air in the alveoli on the one side, and the blood on the other. According to the law of partial tension, the volume per cent. of ether on both sides of the alveolar wall will have a tendency to become equal when ether is administered as a vapor to the lungs. If, for instance, the blood contains five per cent. ether and the air in the alveoli three per cent., ether will be excreted into the alveoli until both the blood and the air in the latter contain the same percentage. If, however, the blood contains less ether than the alveolar air, the blood will then absorb ether until it contains the same percentage as the air of the alveoli. *The concentration of ether in the blood, and therefore, the intensity of action at a given time, is governed not by the absolute quantity administered, but by the percentage contained in the air of inspiration.* The air of inspiration must contain six per cent. in order to produce complete loss of consciousness and insensibility to pain in human beings. Air containing over this percentage tends to paralyze the respiratory centre. When failure of respiration occurs from an overdose of ether, it may be overcome by stopping the administration of this

drug and by applying artificial respiration. These measures favor the excretion and thus lower the concentration in the blood.

When ether is administered slowly by inhalation, its action on the **central nervous system** *may be divided into four stages; in the first, there is a primary decrease of consciousness accompanied by a feeling of asphyxia and ringing in the ears; in the second, the controlling centres in the cerebrum are depressed and there is incoordination of movements and speech which may amount to violent struggling and shouting; in the third, or the stage of surgical anæsthesia, the whole cerebrum and cord are paralyzed, sensation to pain is lost, and there is complete unconsciousness and muscular relaxation; in the fourth, the medulla becomes paralyzed, and asphyxia and weakened circulation ensue. Death takes place in this stage from paralysis of the respiratory centre.*

The **heart** *is never directly stimulated by ether.* The increase in pulse rate seen at the beginning of anæsthesia is purely a reflex phenomenon, due to irritation of the air passages by the ether vapors, yet, in the course of ordinary anæsthesia, the blood pressure is not as a rule much decreased. Poisonous doses produce a marked fall of blood pressure by depressing the **vasomotor centres** and the heart itself; while smaller doses at the beginning of anæsthesia, may produce a short and insignificant rise of blood pressure, due probably to a reflex stimulation of the centre. Concentrated ether vapors may paralyze the heart at the beginning of anæsthesia before the drug has had time to reach the central nervous system. Under these circumstances, the circulation may, at times, be restored by violently compressing the thorax with the object of squeezing out the poisonous blood from the heart and mechanically stimulating this organ.

The **blood** is undoubtedly affected by ether, as the red blood corpuscles become destroyed. After a prolonged anæsthesia, a considerable degree of anemia may be observed by a direct blood count. Nicloux made quantitative determinations of ether in the blood under various stages of narcosis. He found that under light anæsthesia, the blood contained about one hundred mgs.

per 100 c.c., in deep anæsthesia about 130 mgs., while fatal results were obtained when 160 mgs. per 100 c.c. were present. The **bactericidal and phagocytic** action of the blood have been found very much reduced by etherization, even more so than by chloroformization.

Marked **diuretic** effect has been found after from 30 minutes to 4½ hours' etherization. This was greater the longer the ether was administered. It is probably due to a local stimulant effect upon the kidney. This stimulant action may become so great as to cause actual inflammation of the **kidneys** or to increase nephritis if already present.

The **pupils** are somewhat dilated during the stages of primary decrease of sensibility and of excitement. They are *contracted during complete anæsthesia.* Then, they dilate again, either when paralysis of respiration and circulation occurs, or when consciousness returns.

Owing to the great diffusibility of ether, it easily penetrates the skin and mucous membranes, and causes **local irritation;** when its evaporation is prevented, it even produces blisters. When administered by inhalation, it gives rise to irritation of the mucous membranes of the respiratory tract which leads to *increased salivary and bronchial secretion.* Sometimes, especially after prolonged anæsthesia, the inflammation of the lungs may result in pneumonia. The ether which is swallowed produces *irritation of the stomach,* causing vomiting, and the intensity of the gastritis may be great enough to give rise to bloody emesis. The irritation in the nose of the terminations of the trigeminus, and in the throat of the superior laryngeal nerves, may lead to *reflex arrest of the circulation and respiration.* On the other hand, subcutaneous injection of ether, as of any irritant substance, may bring about a reflex stimulation of respiration and circulation, but such stimulation is always of a very transient character. When ether is allowed to evaporate upon the skin, it produces cold and **local anæsthesia.**

Ether does not affect the contractile power of the parturient **uterus** in moderate anæsthesia, but in deeper stages, when very

prolonged, the uterine contractions may become markedly diminished. There is probably no effect upon the fetus except when very large quantities of ether have been given.

CHLOROFORM, which was introduced as a substitute for ether, resembles the latter in its action, but it is about three to four times more powerful and produces general anæsthesia much more quickly. Like the other members of this group which contain halogens, it is much *more depressant to the heart*, and is more likely to cause a sudden arrest of this organ when too concentrated vapors are given. Its toxicity on the frog's heart is thirty-six times greater than that of ether.

The **central nervous system** is affected in the same order by chloroform as by ether, but more intensely by the former, so that anæsthesia is obtained more rapidly and with less chloroform. The stage of excitement is apt to be less marked and often to be absent.

The **circulation** is much more seriously affected by chloroform than by ether. Weakening of the heart is markedly present even in the stage of surgical anæsthesia and the blood pressure is considerably lowered throughout an ordinary chloroform narcosis. This is partly due to a lowered efficiency of the heart itself, but also to a dilatation of the blood vessels due to a direct *paralysis of the smooth muscle fibres* within their walls. Thus vaso-dilatation is not as with ether due to depression of the vasomotor centres.

Another very important action of chloroform upon the heart is the stimulation of the **inhibitory centres** which may cause a temporary or even permanent stoppage of the heart-beat, especially when this organ has been weakened by chloroform. Fatal results from this source may occur at the very beginning of anæsthesia.

The body **temperature** is markedly lowered, sometimes even for many hours after the administration of chloroform has been discontinued, and this fall is due not only to the increased heat expenditure through the skin, but also to the decreased heat production caused by the diminution of the muscular movements and of the oxidative processes of the body.

Chloroform is in a sense a **protoplasmic poison,** as it interferes with the action of many organized and unorganized ferments, and therefore acts as an *antiseptic.* On account of this toxic effect, it causes fatty degenerations of some parenchymatous organs, as the liver and kidneys. Such effects are sometimes seen after prolonged surgical anæsthesia and may simulate yellow atrophy of the liver. Several cases have even proved fatal.

The **red blood corpuscles** have a particular attraction for chloroform and it has been shown that during chloroform anæsthesia the reds contained much more chloroform than the plasma. This drug has a well marked hemolytic action both in vivo and in vitro and is capable of producing a considerable degree of anemia.

The **elimination** of chloroform follows the same order as that of ether, i. e., chiefly by the lungs and a small percentage by the kidneys, but Nicloux has found that a certain small percentage was oxidized in the living body. Small quantities of chloroform have been found in the perspiration and in the milk.

The **local irritant action** of chloroform is a little greater than that of ether, but during or after anæsthesia it is much less evident, as smaller quantities are necessary for an equivalent narcotic effect. Thus, there is *much less salivation and rarely postnarcotic vomiting.* For the same reason, the kidneys are not so liable to irritation during short chloroform anæsthesia.

ETHYL BROMIDE induces anæsthesia very rapidly, and return to consciousness is also very speedy, much more so than with ether or chloroform. Ethyl bromide differs in its action from ether and chloroform in that it *paralyzes the sensation of pain before the production of complete unconsciousness, but the respirations stop from paralysis of the respiratory centre at the same time that the loss of the reflexes and muscular relaxation occur.* The **heart** and the walls of the blood vessels are less depressed than by chloroform. Occasionally in human beings, after apparent recovery from ethyl bromide narcosis, a condition of severe and even *fatal collapse* may suddenly arise. This condition may be reproduced artificially in animals and is probably due to the formation of a

more toxic decomposition product. The substance ethylene bromide, with which ethyl bromide should not be confounded, is exceedingly toxic and produces just such collapse as is observed at times after ethyl bromide.

ETHYL CHLORIDE, like ethyl bromide, is an exceedingly rapidly acting anæsthetic, as unconsciousness may be produced from its inhalation in 2 to 3 minutes. This rapidity of action is probably due to its great volatility, as it boils at 12° C. Recovery is also exceedingly rapid. It produces no general excitement and is very pleasant to inhale. It is much less poisonous to the heart than chloroform.

PENTAL is also a rapidly acting anæsthetic and produces complete unconsciousness some time before muscular relaxation occurs. It may produce marked muscular spasm, tremors and convulsions. It does not seem to have a marked depressant effect upon the heart, yet numerous accidents have occurred during its use clinically.

MIXTURES OF ANÆSTHETICS have been used for many years, mainly on the principle that they might be more active and safer than the single anæsthetics. The first proposition has been borne out experimentally by Honigmann and more recently by Madelung. It has been found that the sum total of the action of two volatile anæsthetics was greater than the arithmetical addition. As regards safety, the mixtures have been a total failure because they introduce a great degree of uncertainty on account of the constant change of the mixture through the different boiling points of their elements. One of the most famous of these mixtures has been the British A.C.E., containing alcohol one, ether two, and chloroform three parts by volume. Another is Schleich's mixture which contains ether, chloroform and petroleum.

NITROUS OXIDE, although not related chemically to this group, is most appropriately described here on account of its pharmacological action, which closely resembles that of the ether series.

When it is **inhaled mixed with air** at the normal atmospheric pressure, it produces flushing of the face, hilarity, for which it was

called laughing gas, unsteady gait and incoordination of thoughts and movements, just as in drunkenness or in the first stages of ether narcosis. *Complete anæsthesia does not take place unless the atmospheric pressure is raised or unless it be given in the absence of air*, because otherwise the concentration in the blood is not sufficient for maximum effect.

When **pure nitrous oxide** is inhaled without admixture of air, the patient passes rapidly through the symptoms just described, then becomes unconscious, and after deep cyanosis, dyspnœic and stertorous breathing, the respirations cease before the circulation.

Nitrous oxide undiluted with air, produces *anæsthesia somewhat similar to that obtained by ether*. Unlike the latter, it produces a rise of blood pressure which is due to asphyxia as it does not occur when air is given with it. Excepting that it does not give rise to convulsive movements, it causes the same respiratory phenomenon which is seen in asphyxia. *It produces: first, a stage of violent inspirations; second, one of violent expirations; third, a few inspiratory movements ending in paralysis of respiration.*

Anæsthesia is obtained in one minute during the second stage of the respiratory phenomenon. It lasts about one minute after the administration of the gas is discontinued. The subject can be revived by artificial respiration even at the beginning of the third stage of the respiratory changes. This fact makes nitrous oxide one of the safest of the general anæsthetics.

When nitrous oxide is given diluted with twenty per cent. of oxygen, but under one and one-quarter of an atmosphere pressure, complete anæsthesia can be obtained and maintained for hours without any ill effects. This demonstrates that nitrous oxide has *specific narcotic properties* like ether or chloroform and that the anæsthesia produced by it is not due wholly to asphyxia. When it is administered in the absence of air, as it is usually employed, there is little doubt then, that the narcosis is due to both specific narcotic properties and to beginning asphyxia, because a very small quantity of air is sufficient to prevent complete anæsthesia.

CHLORAL has almost the same pharmacological action as

chloroform so that it was formerly, but wrongly, thought to be decomposed into the latter in the body. It acts as chloral and is **excreted** in the urine in part combined with glycuronic acid as urochloric acid. Chloral, like the other solids of this group, is less readily absorbed and excreted than chloroform. Therefore, it acts more slowly and for a longer time. On this account the first stage of **narcosis,** i. e., depression of the cerebrum with drowsiness and sleep, can be more easily maintained. However, *larger doses produce complete unconsciousness, loss of reflexes, paralysis of respiration and fall of blood pressure,* the same as does ether and chloroform.

Moderate doses of chloral produce a condition closely resembling normal sleep. The respiration and pulse are slightly slowed and the subject can be awakened by external irritation, as in natural slumber. If the individual is in pain or if the reflexes are greatly exaggerated, very large doses are required to bring about the somnifacient action of chloral, and this is to be explained by the fact that the latter, like the other members of this group, *paralyzes first the higher faculties of the brain and only later the centres governing pain* and the reflex irritability of the cord.

After having taken an ordinary medicinal dose of chloral a patient may wake in from 5 to 8 hours feeling well and refreshed, just as after normal sleep, but sometimes he may suffer from giddiness, vertigo, confusion and headache. After larger doses, as from 4 to 6 grams, the patient falls into a comatose sleep from which he can hardly be aroused, where the reflexes are much diminished and where a condition approaching anæsthesia is present. After such doses there is almost always present headaches, confusion, giddiness, nausea, and vomiting.

Chloral does not paralyze the sensation of **pain** as does morphine in medicinal doses. Sleep may even be completely prevented by the presence of pain.

The efficiency of the **circulation** is markedly affected by chloral. *The blood pressure is lowered by depression of both the vasomotor system and of the motor ganglia in the heart.* The dilatation of the peripheral blood vessels results both from the central ac-

tion and also from a *local effect on the vessel walls*. In consequence of these facts, chloral should be used with great caution when the circulation is previously depressed.

The body **temperature** is decreased on account of the dilatation of the superficial blood vessels, and from an action on the heat regulating centres in the medulla.

The effects of chloral on the **metabolism** correspond very closely to those of chloroform. An augmented destruction of proteids with imperfect oxidation is suggested by the fatty degeneration of various organs, seen after prolonged chloral administration, and also by the increased elimination of nitrogen, phosphates and sulphates.

When chloral is taken in increasing doses over a period of time, a **habit** is contracted just as with morphine, cocaine and alcohol, and the sufferer shows the same general depression, cachexia, digestive disturbances, diminution of mental powers and skin eruptions which are observed in morphine fiends.

Local irritation is a well-marked symptom of chloral on the mucous membrane. It is very apt to produce nausea and vomiting from irritation of the gastric mucosa. For this reason it should always be administered well diluted. Besides the irritant action, it also has a mild **local anæsthetic effect** which is sometimes made use of by skin specialists.

The various **chloral derivatives,** chloralformamide, chloralose, chloretone, hypnal, dormiol, ural, somnal, also butyl chloral and isopral, have an action resembling, to a certain extent, that of chloral.

SULPHONAL, or sulphonmethane, has an *action on the central nervous system, similar to, but less intense than chloral.* In small doses it does not depress respiration and circulation as much as the latter, but it is very apt to produce *irritation of the kidneys*, through which it is excreted partly changed to ethylsulphonic acid. After prolonged use, especially in weak subjects, it may cause hæmatoporphyrinuria, headache, ringing in the ears, nausea, vomiting, weakness, suppression of the urine, skin rashes, disturbances of cerebration and gait, and even collapse and death.

Although the milder **untoward symptoms** are not very infrequent, fatal results seldom occur.

Sulphonal being very insoluble in water is exceedingly *difficult of absorption*, so that its action may not be seen for a great many hours after administration. For instance, this drug given at night for sleeplessness, may not produce sleep until the next day, and since it is very slowly excreted, its effect may last throughout that day.

TRIONAL, or sulphonethylmethane, and **TETRONAL,** resemble sulphonal in their chemical structure, action and uses. Trional acts somewhat more rapidly than sulphonal because it is more soluble in water and more readily absorbed. It is also less likely to produce disagreeable symptoms, although hæmatoporphyrinuria may result from both trional and tetronal.

PARALDEHYDE possesses the general narcotic action of chloral, but it is much *less depressant* to the respiration and circulation: on the other hand it is less efficient in producing sleep. It is excreted mainly by the urine, but also in part by the breath, to which it gives a disagreeable odor. Patients frequently object to paraldehyde on account of its peculiar smell and taste, and these may be sufficient to counterbalance the narcotic effect of the drug. It is usually a very safe hypnotic, and from 50 to 100 G. have been taken without fatal results, although the medicinal dose is about 3 G.

AMYLENE HYDRATE, or dimethylethylcarbinol, is a more powerful hypnotic, but has a greater depressant action on the heart and respiration than paraldehyde, although it does not have as much depressant effect as chloral. In dogs and cats, it produces considerable excitement which may result in convulsions.

URETHANE, or ethyl carbamate, has also a mild hypnotic action. It *does not depress respiration and circulation*, but even stimulates these in small medicinal doses, and for this reason it would be almost a perfect hypnotic if, in some subjects, it did not entirely fail to produce sleep. It is *oxidized in the body to urea.*

VERONAL, although related chemically to urethane, is much more powerful. It may produce poisonous effects from depres-

sion of the respiration and circulation, which in a few cases have resulted in death from collapse; nevertheless, in small doses it has been found very useful as a soporific.

HEDONAL, another urethane derivative, has quite good narcotic properties and is not so depressant to the vital centres as veronal.

BROMURAL, a new derivative of urea, has recently been introduced with claims of being both a nerve sedative and somnifacient. A number of authors find that its effect as a sleep producer is much less marked than as a sedative.

ADALIN acts very much like bromural and is more valuable as a sedative than as a hypnotic. It is said not to produce any by-effects or any unpleasant action upon the heart or respiration when given in smaller doses.

ISOPRAL has been recently introduced as a narcotic by Impens, as being free from untoward effects and much more active than chloral as a narcotic. Others, however, have found it dangerous in some cases and as possessing a number of untoward effects, such as headaches, dizziness, weakness of the limbs, vomiting and skin eruptions.

NEURONAL has been warmly recommended by some as a narcotic with a claim that the sleep was obtained rapidly, was of a restful character and that the waking was unattended by unpleasant symptoms. Nevertheless, numerous other authors have found it to possess marked untoward effects, as burning in the stomach, dizziness and headaches, nausea, vomiting and skin eruptions.

BORNYVAL, GYNOVAL and BROVALOL are preparations of valerianic acid which have been highly recommended recently by their manufacturers as nerve sedatives. Their action is very uncertain, and being volatile oil compounds, their effect is very irritant to the mucous membrane of the stomach and they have not found favor in the author's hands.

ETHYL ALCOHOL exerts the same effects as ether on the central nervous system and circulation, but with very much larger doses. It causes the same local irritant action. *It differs essen-*

tially from ether in being burnt in the body to carbon dioxide and water. It, therefore, *produces heat and energy and can replace a certain amount of carbohydrates and fats in the diet.*

On account of the very extensive use of alcohol as a beverage and as an intoxicant, great attention has been given to its pharmacological action. Very varied opinions have been expressed concerning its utility and effects on the animal organism. *One erroneous statement made concerning alcohol is that it is a stimulant to the central nervous system and circulation, for, direct experiments have never shown any absolute increase in the efficiency of these functions.* The excitement seen after a few glasses of wine, is the result of paralysis of the coordinating centres, resembling that observed in the first stages of etherization. The greater fluency of speech and assurance in speaking is due to the blunting of the judgment and fear, and not to a stimulation of the intellect, because words are frequently misused and expressions ill chosen. In a few instances, when a man is said to do better mental work under the influence of alcohol, it is probable that he has such an excellent intellect that he is accomplishing it rather in spite of this drug.

The special senses are also depressed so that the vision, hearing, taste, smell and touch are all decreased in sharpness of perception. The sense of pain is also numbed and the lack of sensibility to external injuries seen in drunkards, is a testimony to this fact.

Although, after a few glasses of whiskey one may occasionally feel more energetic, still the absolute capacity for **muscular work** is much decreased, fatigue comes on sooner, and recovery from the exhaustion is slower. Direct experiments on the isolated frog's muscles also show a decrease in muscular force. In the training of athletes, it is generally admitted that exclusion of alcohol gives better results, and this fact explains the success of Americans in international matches, because they especially train without intoxicants.

The **heart** is never directly stimulated by alcohol; on the contrary, large doses paralyze its action. This effect can be shown both on the intact animal and on the isolated apex. In the iso-

lated frog's heart it has been found that alcohol is one hundred and ninety-two times less toxic than chloroform. An *increase in pulse rate* is usually observed after a few drinks, but this is chiefly the result of the excitable surroundings, and also, to a smaller extent, of a reflex stimulation from the local irritant effect.

With sufficient quantities the **vasomotor centres** are depressed, the larger blood vessels are dilated and the blood pressure falls, but very small doses are sufficient to dilate the peripheral vessels. This gives the well-known alcoholic reddening of the face and the sensation of warmth. The internal body **temperature** is reduced, especially when that of the external surroundings is very low. As a precaution, people in Arctic regions do not drink alcoholic beverages before exposure to cold, for fear of freezing to death.

A small quantity of alcohol taken internally or injected subcutaneously, usually increases, for a short time, the rate and fullness of the **respirations.** This is purely a reflex phenomenon, as the only direct action of alcohol on respiration is a depressant one.

Contradictory opinions have been expressed on the action of alcohol on **digestion.** The truth is that alcoholic beverages usually *increase appetite* on account of their pleasant taste and local irritant effect on the mouth and stomach. In concentration not sufficient to produce inflammatory reaction, alcohol *stimulates the secretion of the digestive juices*, and when it is diluted enough, it does not decrease the efficiency of the ferments. In concentration of over ten per cent., it retards the action of pepsin. The local stimulation also improves the motor activity of the gastro-intestinal tract: this explains the relief of after-dinner fullness by a small glass of brandy.

Alcohol has a very marked action on the **metabolism** depending on several factors, one of these being the fact that it is oxidized in the living organism to carbon dioxide and water. For instance, when not more than one hundred grammes are given daily to a man, it is all burnt except two per cent. which is found in the urine. Because of its presence in the urine, it markedly

increases **diuresis.** The oxidation, however, takes place rather slowly. Just as with some other oxidizable substances, the *power of an organism for burning alcohol may be increased by* **habit,** so that habitual drinkers can take much larger quantities with less action than those not accustomed to its use.

As might be expected, on account of its combustion in the body, *alcohol can replace carbohydrate and fats in the diet* in isodynamic amounts; so seven grammes of alcohol are practically equivalent to four and one-tenth grammes of carbohydrate or nine and three-tenths grammes of fat. This is only true *when moderate doses are used* and when the individual is accustomed to alcohol. Under such circumstances the proteids are also spared and the amount of nitrogen in the urine is diminished.

When large toxic doses are used, or when it is first given to an individual not habituated to it, *an increase in the proteid destruction* takes place as shown by a great increase in the nitrogen excreted in the urine. This is due to its *poisonous effects on the cellular protoplasm.* This action can be seen on unicellular organisms just as with chloroform, which fact makes both these substances **antiseptics.**

Alcohol, however, is much weaker in its antiseptic power than chloroform, as many bacteria may grow abundantly in a 4 per cent. solution. Concentrated alcohol, or at least of the strength from 60 to 70 per cent., is strongly antiseptic.

Acute poisoning by alcohol presents practically the same picture as the intense action of any of the members of this series, as ether, chloroform or chloral; i. e., the symptoms are those of *gradually increasing narcosis which ends in paralysis of the respiration and circulation.* As mentioned above, the depressant action of alcohol on the heart is much less than that of chloroform, so that, unless there are some previously existing pathological conditions in the heart, death usually results from paralysis of the respiratory centre before the heart is stopped.

Death from acute alcoholism is infrequent, and the **chronic abuse** is a much more alarming factor in civilization. The chronic effects of alcohol are seen in the form of *connective tissue*

formation and degenerations of different organs. The irritation produces, in the throat, chronic pharyngitis; in the stomach, chronic atrophic gastritis. A large percentage of the alcohol ingested reaches the liver and this organ suffers in alcoholics from a degeneration with connective tissue proliferation called cirrhosis. The intellect frequently suffers because of a similar change in the brain leading to the formation of a pachymeningitis. Marked **psychoses** occur from the abuse of alcohol. Many of these take the form of paranoia. Some of the striking symptoms of alcoholic psychoses are delirium with hallucinations of sight and hearing, retrograde amnesia, etc. The peripheral nervous system is also affected with the development of neuritis, with pain in the limbs, tremors and paralysis. The toxic effects on the metabolism may predispose to gout, arteriosclerosis and contracted kidney.

Methyl Alcohol, otherwise known as wood alcohol, is of no importance in therapeutics, but it has become very interesting of late on account of numerous cases of poisonings arising from its use. The source has been from the adulteration of ethyl alcohol or from patent medicine containing this product. It is much more poisonous than ethyl alcohol, and this is probably because it is oxidized to formic acid and formic aldehyde, which are themselves poisonous. Besides the symptoms of narcosis, this drug produces very marked local irritant action and also convulsions. It not infrequently causes optic neuritis with atrophy and blindness.

SUMMARY OF THE GROUP ACTION.—*The central nervous system is depressed in the following order, brain, cord and medulla. The heart is never directly stimulated but depressed with large doses, and especially by members containing halogens, as chloral and chloroform. Local irritation is well marked and may give rise to reflex influences on respiration and circulation.*

THERAPEUTIC APPLICATION.—The main use of the members of this group is derived from their depressant action on the brain and cord. They may be used according to the dose, either to depress mildly the cerebrum and thus to produce sleep, or to

paralyze completely the cerebrum and cord and thus induce complete loss of consciousness and of the reflexes, also to cause insensibility to pain.

Anæsthesia, or the complete loss of consciousness produced to enable the performance of painless surgical operations, is more appropriately brought about by the gaseous or very volatile liquids of this group. These are easily absorbed and easily excreted so that the intensity of action can be conveniently regulated. The so-called anæsthetics, include *ether*, *chloroform*, *nitrous oxide*, *ethyl bromide*, *pental*, etc.

To *induce simple sleep*, the solids, or the less easily volatilized liquids are best adapted because of their slower absorption and excretion. Their action is more prolonged, but becomes less rapidly intense. The chief members of this division, sometimes called that of hypnotics or soporifics, are *chloral*, *sulphonal*, *tetronal*, *trional*, *veronal*, *hedonal*, *urethane*, *paraldehyde and alcohol*.

Sleep is, like the waking state, an active condition of the living organism. Its purpose is to rest the tired cells in order that they may not become the prey of auto-intoxication. Different conditions are important in the occurrence of sleep. These are limitation of voluntary movements, an abstract state of the mind or a monotonous stimulus, also a lowering of the general reflexes. Such drugs as the bromides, to be considered in a subsequent group, help in the production of sleep by decreasing the ingoing stimuli and limiting voluntary motion. The drugs of the chloral group, on the contrary, act by decreasing the functional activity of the brain. It can easily be seen that the sleep produced by these drugs is different from normal sleep and is akin to a partial paralysis of the brain. It is for this reason that in spite of the claim of manufacturers, all are prone to produce unpleasant symptoms on awaking just as after having taken an excess of alcohol, and instead of feeling refreshed patients frequently feel tired, dizzy, nauseated, etc.

The most powerful, rapidly acting and reliable is **chloral.** It has been accused of being the most depressant drug of the group towards the circulation and respiration, yet when used in small or

moderate doses it does not seriously affect these functions unless they are already depressed by disease. It is quite irritant to the mucous membrane of the stomach and therefore should be administered in a watery solution well diluted with water or preferably with milk. The best method of prescribing it is in the form of a syrup containing about 0.5 G. or 7 grains to the teaspoonful. One teaspoonful may be given ½ hour before bedtime and repeated in 2 hours if sleep has not occurred. On account of its great irritant action it should never be given in the form of tablets, powders, or capsules. This drug or any other of this group should not be used to produce sleep unless sleeplessness has become a dangerous symptom which can not be controlled by the simple sedatives of the bromide group or by hydro-therapeutics, general hygienic measures, etc. The most valuable indications for the use of chloral are in maniacal or alcoholic delirium, or in convulsions of all sorts, as in strychnine poisoning and tetanus. Chloral has also been found valuable in lessening the pains of labor and in affording sleep during the middle of prolonged parturition. Great caution should be exercised in the use of chloral or, in fact, any other narcotic of this group when there is present organic weakness of the heart.

It was formerly asserted that sulphonal, veronal, but especially paraldehyde and urethane were perfectly safe drugs, but all have against them a record of deaths following their administration.

Sulphonal, tetronal, trional, veronal, neuronal, isopral, etc., have all been prescribed chiefly in powder or tablet form on account of their rather difficult solubility in water: their ingestion should be followed by a hot drink, particularly an alcoholic one, because this aids their absorption. They also should be given 1 or 2 hours before sleep is desired as their action is much slower than that of chloral. They have also a well-marked irritant effect upon the stomach, like chloral, and may produce nausea and vomiting.

Ethyl carbamate or urethane being very soluble in water, is best given in the form of a watery solution or syrup containing 1 G. or 15 grains to the teaspoonful. It is one of the safest mem-

bers of this group, but unfortunately is often not powerful enough to produce sleep except in very large doses.

Paraldehyde having such a bad taste and odor is best given in the form of an elixir containing 2 c.c. or 30 minims to the tablespoonful. It is a fairly safe hypnotic if too large doses are not used, but like ethyl carbamate it frequently fails to produce sleep.

Alcohol is used in medicine both internally and externally. Its external use is by virtue of its irritant and bactericidal action. As an irritant it is employed to stimulate the circulation of the skin either over the whole body or local parts. As an antiseptic it is employed very much more nowadays than in the past, and in fact many surgeons use it exclusively for the disinfection of the abdomen before laparotomy and also for the sterilization of some surgical instrument.

Internally it is used to some extent, but less than in the past, as a narcotic in cases of sleeplessness. For this purpose the common alcoholic beverages, as ale, beer, porter, are generally employed. It is used as a gastric stimulant in anorexia in cases of nervous fatigue and atony of the stomach in the form of some alcoholic beverages before meals. It is also employed, but less than in the past, in febrile diseases, as pneumonia and typhoid fever. The general impression among physicians is that its good effect in these and similar diseases is derived from a stimulant effect upon the heart. This impression is erroneous and the good probably comes from its virtue as a food.

General anæsthesia is used chiefly for the performance of surgical operations, for painful examinations, or in labor.

The apparatuses used for administering anæsthetics differ to a considerable extent according to the choice, but there are certain general principles which govern the use of all volatile anæsthetics and these are based upon the laws of partial pressure of gases. As it has been found experimentally that certain definite proportions of the various anæsthetics are required to produce anæsthesia, methods have been devised of making definite mixtures of the anæsthetics with air or oxygen. All forms of inhalers, from the very simplest to the most complicated, are in use.

Preliminary to anæsthesia, a patient should be very carefully examined and if she shows evidence of marked myocarditis it is dangerous to proceed, especially with chloroform, which may produce degeneration of the heart's muscle. If marked arteriosclerosis is present both ether and nitrous oxide are contraindicated because they both may cause a temporary increase of blood pressure. Bronchitis, colds or any irritation of the lungs make the patient a little more liable to anæsthetic pneumonia. Ether is much more dangerous in this respect than chloroform. Advanced Bright's disease or diabetes contraindicate both ether and chloroform. Marked anemia is also an undesirable condition in which to give any anæsthetic.

The problem of **practical anæsthesia** is by no means a simple one and in England and recently in America the best surgeons realizing this fact employ only trained anæsthetists. The general principles are as follows: the stomach and intestines should be as nearly empty as possible. The intestines may be cleaned by a high enema the night before operation and the stomach should have only received easily digestible food the night before the operation and a small quantity of light liquid nourishment a few hours before. Great care should be exercised to see that the patient has no false teeth or other foreign objects in his mouth and also that his clothing is loose all about the body so as not to interfere with his respiration, also that he is suitably covered with blankets or warm water bottles in order that he will not suffer lowered resistance by cold. In the case of ether or chloroform, when given by the open method not previously mixed in a tank with oxygen, they should be administered on a light permeable inhaler held some distance from the face while the eyes are kept closed to prevent their irritation. Great care should be taken that the cone is not too near the face when the patient takes a deep respiration. Also when anæsthesia is very advanced that the patient is not choked by swallowing his tongue or by inhaling vomitus or mucus. The tongue can be pressed forward by pushing on the angles of the jaw or by pulling out this organ with a towel or forceps. Mucus or vomitus may be re-

moved by turning the head to one side and sponging out the mouth with gauze. If during anæsthesia there is sudden arrest of *respiration* this may be remedied by removing the anæsthetic and giving respiratory stimulant and artificial respiration. Should the heart fail, due to inhibitory stimulation, the treatment consists of inverting the patient and giving massage of the heart and artificial respiration. Atropine may be found useful, as it paralyzes the inhibitory mechanism, and is best administered by direct injection into a vein or into the heart itself.

During the past few years many arguments have been adduced both for and against the *use of some narcotic before general anæsthesia*. The purpose is to ease the stage of going under the anæsthetic and also to permit a smaller amount of the same to be used. For a long time it was recommended to give atropine in order to prevent the disagreeable excessive bronchial mucus. In recent days, the hypnotics of the chloral group, as chloral itself, hedonal and veronal, have been urged as adjuvants to the anæsthesia. The best method of preparation is undoubtedly the administration of morphine $\frac{1}{3}$ grain and scopolamine $\frac{1}{120}$ of a grain 1 to 2 hours before anæsthesia. This procedure in itself has been followed by complete anæsthesia and it undoubtedly decreases enormously the amount of the volatile anæsthetic which has to be employed. It also decreases the amount of bronchial mucus and the chances of inhibitory arrest of the heart by means of scopolamine which acts in many respects like atropine.

For general anæsthesia the drugs most commonly employed at the present time are **ether** and **chloroform.** The anæsthesia with ether or chloroform is usually preceded, if not by morphine and scopolamine, by the use of some much more rapidly acting volatile anæsthetic, as nitrous oxide, ethyl chloride, etc. Chloroform is by no means unpleasant and can be used from the beginning, but with ether it is positively barbarous to begin anæsthesia with this substance as it is so unpleasant and takes so long to produce unconsciousness unless pushed dangerously fast. Ether anæsthesia may be begun with chloroform.

Other methods, besides inhalation of volatile anæsthetics, have been devised and used practically in recent days. They comprise rectal, intravenous, intratracheal and intramuscular anæsthesia.

Rectal anæsthesia with the use of ether or chloroform was first introduced over twenty years ago, but was soon abandoned at that time because the introduction of ether in substance, or of too concentrated ether vapors, caused alarming inflammation of the intestines. Within the last few years, Cunningham revived this method, using ether vapors laden with watery vapors, well diluted and heated at the temperature of the body. By this method and the use of a very simple apparatus, he and others were able to carry out rectal ether anæsthesia with only rare evidence of intestinal irritation. The advantages claimed by Cunningham were, that rectal anæsthesia permitted more easily of operative procedures about the face, was pleasanter to take and seldom produced nausea and vomiting. In using this method a careful examination of the intestines by abdominal palpation, sigmoidoscopic and fecal examination should be made, as one death was reported, due to rupture of an amebic ulcer.

Intravenous anæsthesia with ether and chloroform was introduced by Burkart a few years ago and used by him both in animals and on human beings. He conducted the anæsthesia by running into a vein of the arm at a very slow rate, a solution of ½ per cent. chloroform or 5 per cent. ether. The duration of the infusion lasted about one hour. This author obtained no ill effects, such as headaches, nausea, vomiting. In a few patients, there was evidence of slight renal irritation. The object of this method was to facilitate operations about the head and also to overcome the disagreeableness and post-narcotic symptoms present after inhalation anæsthesia.

Since Meltzer and Auer demonstrated the possibility of **intratracheal anæsthesia** upon animals, several anæsthetists and surgeons have worked to apply this method upon human beings. While in animals tracheotomy is performed, in human beings a catheter is introduced into the larynx and trachea, just as the intubation apparatus for diphtheria. The ether vapors diluted

with air or oxygen, likewise nitrous oxide oxygen mixtures, are pumped rhythmically into the lungs. Cotton, Boothby, and Ehrenfried have perfected an apparatus simplifying this method and report very favorably on the result obtained. The chief claim for the introduction of this method is on the ground that it is much safer than the inhalation method and that it can be more easily controlled, since if too much anæsthetic has been taken, in a moment pure oxygen can be introduced into the lungs rhythmically and thus revive the subject.

Recently, in Paris, **intramuscular** ether anæsthesia has been placed in practical operation. The amount of ether required was about the same number of c.c.'s as kilo weight of subject.

Ether and **Chloroform** are the two commonly employed to bring about complete *anæsthesia during major surgical operations*. It requires a much longer time to produce unconsciousness with ether than with chloroform. Ether causes more marked vomiting and irritation of the respiratory tract because much more of this drug has to be used to produce the same narcosis as with chloroform. On the other hand, ether is less depressant to the circulation and less liable to produce fatty degeneration of parenchymatous organs than chloroform. The former is better adapted when there is a disease attended with decreased strength of the circulation or parenchymatous degeneration of certain organs.

Ether and chloroform have been used in the form of waters, spirits, emulsions, etc., by virtue of their local anæsthetic action in painful *functional affections of the stomach*. They are not well adapted for organic diseases of this organ because of the irritation which they produce.

Ether and chloroform are used in the form of liniments as *counterirritants* on the skin over diseased parts, such as rheumatic joints. Here their beneficial action is probably due to reflex changes in the circulation and metabolism of the affected part.

Ethyl bromide cannot be used as an anæsthetic in major surgical operations, because complete surgical anæsthesia with muscular relaxation cannot be obtained without death of the pa-

tient, since the centre of respiration is paralyzed at the same time that the reflexes are abolished. It can only be used when short and incomplete anæsthesia can be of service, such as for *opening abscesses* or in small *gynæcological operations*, or in *parturition*.

It is usually administered by saturating a cone with about 30 c.c. or 1 fluid oz. and kept over the face until anæsthesia results.

Ethyl chloride which has a very low boiling point (12° C.) has been used for many years to produce local anæsthesia by freezing. It is kept in sealed tubes and sprayed over the part to be operated until it becomes anæsthetic from the cold. More recently, however, it has been reintroduced as a general anæsthetic by inhalation. It has some very decided advantages. Firstly, it is very rapid in its action, producing loss of consciousness within two to three minutes. It has not proved dangerous when employed in small amounts. Its effect is very fleeting because of its low boiling point and, therefore, is not as practical as others for prolonged anæsthesia. Its chief indication is for short anæsthesia or for beginning anæsthesia to be continued by other anæsthetics.

Nitrous oxide has not received much attention as an anæsthetic in major surgical operations until the last few years. However, since its discovery by Wells, it has been enormously employed for short anæsthesia to enable the performance of minor surgical operations, such as pulling of teeth, opening abscesses, dilatation of the anal sphincter, and to begin anæsthesia which is to be continued by ether or chloroform or other more powerful anæsthetics. For short anæsthesias, it has been employed in the absence of air so that the anæsthesia came very quickly but lasted but a very short time.

Many years ago, Paul Bert demonstrated the feasibility of giving nitrous oxide for major surgical operations provided that it was administered under pressure and with 20 per cent. oxygen. Until recently this method was not found very practical, because of the cumbersome apparatus needed. Lately, several American surgeons and anæsthetists have worked to simplify

methods and apparatuses for the use of nitrous oxide in major surgical operations. One of the most successful and enthusiastic has been Crile of Cleveland, who has used it in hundreds of cases for all sorts of major surgical operations, lasting, in some cases, over periods of hours, with most excellent results. The claim in favor of nitrous oxide as compared with ordinary ether anæsthesia is that it is less dangerous, much pleasanter to the patient, much more rapid in its action, and producing less shock. In a comparative series of over five hundred cases, Crile found that vomiting followed nitrous oxide in only 17 per cent. of cases, while it followed ether in 42 per cent.

MATERIA MEDICA.

(a) Anæsthetics.

Æther (U.S.P.,* B.P.)*, light, colorless, inflammable liquid, consisting of 96% of absolute ether, with a peculiar penetrating odor and burning taste, boiling at 38° C., miscible with alcohol, chloroform and fats, soluble in 10 parts of H_2O. Its vapors are heavier than air and are highly inflammable. **Dose:**—0.3–2.0 c.c. Br. (8–15 ♏.) Average (U.S.P.) **1.0 c.c.**

Spiritus Ætheris Compositus (U.S.P., B.P.) (Hoffman's Anodyne) consists of about one-third ether with the balance of alcohol and ethereal oils. **Dose:**—1.0–4.0 c.c. Br. (½–1 fl. ʒ.) Average (U.S.P.) **4.0 c.c.**

Chloroformum (U.S.P., B.P.) heavy, colorless, non-inflammable liquid with a pleasant odor and burning sweet taste, consisting of about 99% absolute chloroform, boiling at 62° C., miscible with ether, alcohol and fats, soluble in 200 parts of H_2O. **Dose:**—0.1–1.0 c.c. Average (U.S.P.) **0.3 c.c.**

Emulsum Chloroformi (U.S.P.) contains 4 per cent. chloroform. **Dose:**—5.0–15.0 c.c. Average (U.S.P.) **8.0 c.c.**

Spiritus Chloroformi (U.S.P., B.P.) contains 6 per cent. chloroform. **Dose:**—2.0–5.0 c.c. Br. (½–1 ʒ.) Average (U.S.P.) **2.0 c.c.**

Aqua Chloroformi (U.S.P., B.P.) contains ½ per cent. chloroform. **Dose:**—5.0–15.0 c.c. Br. (1–3 fl. ʒ.) Average (U.S.P.) **16.0 c.c.**

Linimentum Chloroformi (U.S.P., B.P.) contains 30 per cent. chloroform.

Æthylis Bromidum, light, colorless, inflammable liquid, soluble in organic solvents, easily decomposed by light and air, boiling at 38° C. **Dose:**—10–20 c.c. by inhalation.

Pentalum, light, colorless, inflammable liquid, boiling at 38° C.

Æthylis Chloridum (U.S.P.), light, colorless liquid, boiling at 12° C. Kept in tubes under pressure. Used as a spray to produce local anæsthesia.

Nitrous Oxide, colorless gas, without odor, but with a sweet taste, soluble in water. It is kept in tanks under pressure.

*(U.S.P.) means that a drug is described in the United States Pharmacopœia.

*(B.P.) means that a drug is described in the British Pharmacopœia.

(b) **Hypnotics.**

(1) **Chloral Division.**

Chloralum Hydratum (U.S.P.) or Chloral Hydras (B.P.), sometimes called chloral is hydrated trichloraldehyde, composed of colorless crystals, melting at 58° C., with a sweet pleasant odor and a burning taste, soluble in water, alcohol and ether. It is liquefied when rubbed with equal parts of camphor, thymol, menthol or phenol. **Dose:**—0.3–1.0 up to 5.0 G. in 24 hours. Br. (5–30 grains.) Average (U.S.P.) **1.0 G.**

Butyl Chloral Hydras (B.P.) resembles chloral closely. **Dose:**—0.3–1.0. Chloralformamide, chloralose, chloretone, hypnal, dormiol, ural and somnal are chloral derivatives resembling it in its action and uses. **Dose:**—0.3–1.0 G. Br. (5–15 grains.)

(2) **Sulphonal Division.**

Sulphonmethanum (U.S.P.) or Sulphonal (B.P.) and **Sulphonethylmethanum** (U.S.P.) or Trional and **Tetronal,** three sulphon derivatives, are white crystalline bodies only soluble in a few hundred parts of water, but readily soluble in hot alcohol. **Dose:**—0.3–1.0 G. Br. (15–30 grains.) Average (U.S.P.) **1.0 G.**

(3) **Miscellaneous Division.**

Paraldehydum (U.S.P., B.P.), colorless liquid with a disagreeable odor and burning taste, soluble in alcohol and ether, soluble in 8 parts of water. **Dose:**—1.0–5.0 G. Br. (15–30 ♏). Average (U.S.P.) **2.0 c.c.**

Amylene Hydrate, colorless liquid, soluble in water and alcohol. **Dose:**—1.0–2.0 G.

Æthylis Carbamas (U.S.P.) or urethane, white crystals, soluble in water and alcohol. **Dose:**—1.0–2.0 G. Average (U.S.P.) **1.0 G.**

Hedonal and **Veronal** are urethane derivatives, difficultly soluble in water. **Dose:**—0.3–1.0 G.

Alcohol (U.S.P.), colorless, inflammable liquid, miscible in water, ether, and chloroform, and contains 92.3 per cent. absolute alcohol by weight. It has a pleasant odor and burning taste.

Spiritus Rectificatus (B.P.) contains 90 parts pure alcohol by volume.

Alcohol Dilutum (U.S.P.), 41.5 per cent. alcohol, balance H_2O.

Spiritus Frumenti (U.S.P.), whiskey.

Spiritus Vini Gallici (U.S.P., B.P.), brandy.

GROUP OF AMYL NITRITE.

Amyl nitrite and other nitrites form a group of drugs whose pharmacological action is probably due to the nitrous acid radicle.

AMYL NITRITE has a marked effect upon the circulation. *It lowers greatly the blood pressure by paralyzing the smooth muscles in the walls of the internal blood vessels.* At first, it only causes a dilatation of the superficial vessels, especially those of the face and upper part of the body, so that the skin becomes hot, reddened, suffused, and covered with perspiration; it also dilates

the vessels of the head, including those of the meninges, producing a throbbing sensation in the head and neck. It even raises the blood pressure in this stage and only decreases it later when the internal vessels are paralyzed.

To compensate for the diminished blood pressure, the **heart** *increases in rate, although not in force;* the pulse is full and bounding, because the relaxed condition of the vessel walls greatly favors the transmission of the impulse. With sufficient doses, the *heart muscle becomes depressed, and both the rate and force of this organ are decreased, until complete arrest occurs.*

The body **temperature** is lowered on account of the increased loss of heat through the dilated cutaneous blood vessels.

When directly applied, amyl nitrite paralyzes both striped and unstriped **muscles,** but mainly the unstriped and especially those of the blood vessels.

It induces changes upon the **nervous system,** that may be seen even after medicinal doses, in the forms of giddiness, vertigo, disturbances of vision and hearing, and even unconsciousness. In large toxic doses, it produces the same effects upon the **central nervous system as** the members of the ether and chloroform group, i. e., *depression of the cerebrum, spinal cord, and medulla.*

Respiration is at first slightly increased in force and rhythm, but with larger doses it is depressed and finally arrested. The primary increase in respiration is a reflex phenomenon, dependent upon the local irritant action of the drug. Other evidences of **local irritation** seen after inhaling amyl nitrite, are coughing, watering of the eyes, and occasionally nausea and diarrhœa.

The **blood** is profoundly affected and after large doses, *methæmoglobinæmia appears,* giving to this tissue a chocolate brown color, and to the skin, a cyanotic appearance. Since the oxygen in methæmoglobin is not easily available for vital oxidation, death may take place from asphyxia.

The **urinary flow** is not usually increased as was formerly supposed, and on account of the fall of blood pressure, it may even be decreased or arrested. *Part of the nitrite radicle administered becomes oxidized in the body to a nitrate; another portion is possibly*

reduced to ammonia; still another portion remains unchanged, and is found in the urine in the form of alkaline nitrites.

ETHYL NITRITE and other organic nitrites, resemble closely amyl nitrite in their action, but as a rule are weaker.

SODIUM NITRITE, and other inorganic nitrites, possess the same general action as amyl nitrite, but being solids, they are less readily absorbed, therefore, *their action is slower in appearing, but more prolonged.*

NITROGLYCERINE, or trinitrate of glycerine, which is slowly *broken up in the body with the formation of nitrites, nitrates and glycerine,* has essentially the same action as the nitrites. Because it is rapidly absorbed, the effect soon appears, and as it is slowly decomposed, the same is prolonged. It is much more apt to produce *severe headaches* than the other members of this group. These, and the *convulsions* observed in the lower animals, may be due to the action of the nitroglycerine group before decomposition.

Cases of **poisoning** by nitroglycerine from inhalation of dynamite smoke, or from handling of this product, show symptoms very similar to those produced by amyl nitrite, as reddening of the upper extremities, knocking in the head, dizziness, sometimes loss of consciousness, headaches and convulsions. The two latter symptoms are seen more markedly with nitroglycerine. In isolated heart experiments, this drug is found to relax the heart contracted by digitalin.

SUMMARY OF THE GROUP ACTION.—*At first, dilatation of the superficial blood vessels with blushing of the face and neck, later, dilatation of the internal vessels, with fall of blood pressure. With larger quantities, paralysis of the central nervous system in the same order as from ether, therefore narcotic effect, also, depression of the heart muscle and methæmoglobinæmia.*

THERAPEUTIC APPLICATION.—Amyl nitrite was first introduced in medicine, by Brunton, for the treatment of *angina pectoris,* on the theory that the spasmodically contracted vessels in the heart are relaxed by the depressant effect of this drug on the vessel walls. It is certain that the agony of an attack of angina

pectoris is frequently shortened by the inhalation of a few drops of amyl nitrite. **Nitroglycerine** is also employed for the same purpose. The **inorganic nitrites** are not so applicable during anginal attacks, because they act too slowly.

The **nitrites** are sometimes used to lower the blood pressure, and thus relieve the work of the heart in cases of *arteriosclerosis*, when this organ is laboring against too high blood pressure. They are employed in *epilepsy* and *migraine*, on the theory that these conditions may be due to spasmodically contracted blood vessels in the brain. On account of their depressant action on smooth muscle fibres, they are given in *asthmatic attacks*, to relieve the supposed spasm of the smaller bronchi.

Ethyl nitrite in the form of sweet spirits of nitre, has been used for many years to increase the flow of urine and sweat. It has but little action on the urine, but under favorable conditions it may well produce *sweating* by dilating the cutaneous blood vessels.

MATERIA MEDICA.

Amylis Nitris (U.S.P., B.P.) ($C_5H_{11}NO_2$) yellow, volatile, liquid with a strong odor of banana and a burning taste, soluble in alcohol and ether. It contains 80 per cent. of absolute amyl nitrite, the balance being composed of by-products. It is usually dispensed in glass pearls which can be broken in a handkerchief and inhaled during attacks. **Dose:**—0.1–0.3 c.c. Br. (1–5 ♏). Average (U.S.P.) **0.2 c.c.**

Spiritus Ætheris Nitrosi (U.S.P., B.P.), clear, mobile, slightly yellow liquid, with a sharp burning taste and an ethereal odor, which contains 4% of ethyl nitrite, and the rest alcohol. **Dose:**—1.0–5.0 c.c. Br. (20–90 ♏). Average (U.S.P.) **2.0 c.c.**

Spiritus Glycerylis Nitratis (U.S.P.) or Liquor Trinitri (B.P.), colorless liquid, with smell and taste of alcohol, consisting of 1 part nitroglycerine to 99 parts alcohol. **Dose:**—0.06–0.1 c.c. Br. (½–2 ♏). Average (U.S.P.) **0.05 c.c.**

Tabellæ Trinitriti (B.P.), contains 0.0006 G. ($\frac{1}{100}$ grain) nitroglycerine. **Dose:**—1–2 tablets.

Sodii Nitris (U.S.P., B.P.) ($NaNO_2$) white crystalline body, soluble in water. It is deliquescent and gradually changed to sodium nitrate when exposed to the air. **Dose:**—0.1–0.3 G. Br. (1–2 grains). Average (U.S.P.) **0.065 G.**

GROUP OF MORPHINE.

Among the Ancients, the poppy was the emblem of sleep, and for centuries opium in some form has been used in different countries as an intoxicant and as a sleep producer. Just as for alcohol, and in fact for all intoxicants, it is claimed by those who are habituated to its use, that they derive marked pleasure from it.

This group is composed chiefly of alkaloids extracted from the opium poppy, morphine, being the most prominent member, and, the one to which opium chiefly owes its activity.

MORPHINE, *by a depressant effect on the* **cerebrum,** *relieves pain and produces sleep, and when administered to an animal, loss of the sensation of pain is the first action observed.* This is followed by drowsiness which soon passes into sleep, from which the subject can at first be aroused. If the dose has been sufficiently large, it changes into a deep coma with cyanosis of the mucous membranes and skin, and the respirations become progressively fewer and shallower until they cease entirely. Even with small doses, as might be used in practice, morphine greatly lowers the respiratory capacity, and with sufficiently large ones, it produces *death by paralysis of the centre of* **respiration** in the medulla.

Unlike the members of the chloral group, it *increases the* **reflex irritability** of the cord in the lower animals, although in man, depression of the cerebrum is more marked than stimulation of the cord, so that, as a rule, in the latter only a sedative action follows the use of morphine. In some lower animals such as frogs, and occasionally in human beings with an idiosyncrasy towards morphine, it produces excitement and actual convulsions by stimulation of the cord. After awaking from morphine sleep, there may be noticed in man, more or less nausea or vomiting and depression, and occasionally headache and excitement. In dogs, morphine practically always produces **vomiting** within ten to fifteen minutes after subcutaneous administration. This effect is probably due to stimulation of the vomiting centre just as after apomorphine. The **muscles** and **peripheral nerves** are not affected by morphine except when applied in overwhelming amounts, and this drug is in no sense a local anæsthetic.

Morphine, in human beings, does not depress the **heart** nor the vasomotor centre governing the internal blood vessels except in very excessive doses. Thus, the *blood pressure and pulse may remain normal when there is already profound narcosis and depression of respiration;* and in fact, death may occur with the blood pressure but little changed. The cutaneous blood vessels are, however, markedly dilated and this causes redness of the **skin,** sweating and itching. The congestion of the skin by the chronic use of morphine may even produce eczemas which are frequently observed in the habitués of this drug.

Probably through its action on the central nervous system, morphine decreases all **secretions** except sweat. The bronchial and intestinal secretions are the most affected. The **peristalsis** of the gastro-intestinal tract is also diminished so that constipation is often produced; in human beings having an idiosyncrasy toward this drug diarrhœa may occur by stimulation of the cord. Recently it has been found by Magnus that morphine delays the emptying of the **stomach,** from six to seven hours longer than usual, because of spasm of the pylorus. The **pupils** are contracted by central stimulation until just before death from asphyxia when they become widely dilated.

In subjects upon which morphine has a depressant action, the **metabolism** is reduced, as is also the heat production, and on account of the diminution in the respiration, there is imperfect oxidation and in consequence lactic acid and sugar may be found in the **urine.** Otherwise this secretion remains unaffected, although retention may occur in the bladder, due to the loss of normal reflex of urination.

It is chiefly **excreted** *unchanged by the mucous membrane of the stomach and intestines* and so rapidly, that it may be detected in the stomach even in a few minutes after subcutaneous administration, and about forty per cent. of the quantity given is thrown out into this organ within an hour. The rest is excreted by the bowels, as under normal conditions but a small part of the morphine ingested is oxidized to oxidimorphine, which appears in traces in the urine. *When, however, slowly increasing doses are*

given to a subject, the latter acquires the power of oxidizing progressively larger quantities of this drug, and whereas normally over seventy per cent. is found in the feces, in habitués, only traces may be recovered. Experiments have shown that the brain of animals habituated to morphine have a much greater capacity of oxidizing this drug than a normal brain. This would explain the immunity.

When morphine is taken for a certain length of time, a growing desire to continue its ingestion arises. After the **habit** is acquired, the sudden withdrawal of the accustomed dose produces very disagreeable symptoms, which consist of a craving for the drug, often, of diarrhœas, great depression, and even collapse.

Morphinism, is usually attended by the following symptoms; depravity of the mind, general debility, loss of weight and appetite, loss of sexual powers, sleeplessness, eczemas, contracted pupils, diarrhœa alternating with constipation and finally, death from malnutrition.

In **acute morphine poisoning,** the rational treatment consists of emptying the gastro-intestinal tract where morphine is excreted, by repeated stomach washings and by the administration of purgatives. The respiration should be stimulated by respiratory stimulants, and, if necessary, artificial respiration should be performed. The **treatment of chronic morphine poisoning** should consist of a gradual withdrawal of the drug, of improving the nutrition by suitable measures, and of treating symptoms as they arise.

CODEIN is an alkaloid of opium which has similar, but less intense action, than morphine. It usually does not constipate, nor diminish the bronchial secretions, neither does it produce a habit, as does morphine. It increases reflex irritability more, and *decreases the sensation of pain and consciousness less* than the latter drug; although in man, in ordinary doses, no increase in the reflexes occurs. The sleep obtained by medicinal doses of codein is much less profound than that of morphine and the patient usually wakes up easily. When much pain is present, codein is as a rule absolutely inadequate in affording relief.

In order to overcome some of the objectionable features of morphine, various **artificial derivatives** of this substance were made. The most important are **Dionin** and **Peronin,** which have an action closely resembling that of codein. **Heroin** depresses the respiratory centre very profoundly, even more so than morphine itself, yet it does not decrease pain nearly as much as the latter. More recently, there was introduced a crystalline mixture of all the alkaloids of opium called *pantopon* with the claim that it was much more efficient than crude opium or any single one of its alkaloids. This, however, has not been absolutely borne out.

CANNABINOL, the active principle of cannabis indica, has narcotic properties resembling those of the alkaloids of opium, and preparations of the crude drug called Hashish or Bhang, have been used for centuries in India in the same way that opium has been used by the Turks. The East Indians claim, that under its influence they are thrown into a sleep accompanied by the most delicious erotic dreams, but the Caucasians experience only as a rule a general feeling of comfort and well-being and rarely delusions. Occasionally, the dreams are of a disagreeable character and the patient awakes with great depression, nausea and vomiting as may occur after taking morphine. The hallucinations sometimes present, consist of creeping sensations in the hands and feet, also a feeling as if the individual were swimming or flying.

Death has seldom occurred in man after taking even very large doses of cannabis indica. The most marked symptoms of poisoning which have been observed, consisted of great *quickening of the pulse, weakness, general loss of strength, convulsive contractions of the extremities and trismus, and lastly, sleep from which the patient completely recovered.*

Animals are not very susceptible to cannabinol, for rabbits may take five grams by the stomach without any symptoms, although dogs are more susceptible, yet never die from its effect. The symptoms which they show, consist of restlessness followed by somnolence. With large doses, the animal lies unconscious

on the floor, taking deep stertorous respirations and occasionally having muscular twitchings. Vomiting frequently occurs in both dogs and cats.

The **reflex irritability** is first increased then diminished in frogs; the **pulse** is as a rule accelerated in man, due to the exalted psychical condition, but in animals it is usually slowed by stimulation of the vagus and by action on the **heart** itself. This organ stops even before respiration after subcutaneous administration in animals.

Dogs become easily accustomed to cannabinol, so that perfectly enormous doses may be taken without symptoms. The **chronic use** of cannabis indica preparations in the East is occasionally accompanied by *mental derangements*, and the profound disturbance of nutrition seen after opium is also observed in the habitués of Hashish, although many East Indians take it in small quantities during their entire life without any symptoms.

Cannabinol, like morphine, greatly **decreases the sensation of pain** and may entirely suppress it with large doses. It has also less effect upon the sense of touch.

PELLOTIN is an alkaloid obtained from a Mexican cactus, which is made into a beverage and drunk by the natives. It produces pleasant sensations, somewhat on the order of those which the East Indian experiences from Hashish. It has well marked **narcotic action,** but *does not decrease the sensation of pain* as does morphine, resembling more in this respect the narcotics of the chloral group. It has a depressant action on the **respiratory centre** and also upon the **heart,** the latter being slowed in beat and decreased in force. The other alkaloids accompanying pellotin in this cactus, have more or less marked narcotic properties, but one of them, mescalin, produces great excitement and exaltation, such as the perception of brilliant colors and so forth, and is probably the principle to which Pellote or Mescale the Mexican beverage owes its exciting properties.

LACTUCARIUM, or an extract of lettuce juice, has been used considerably as a narcotic, but no basis for this employment has ever been discovered in scientific experiments.

PISCIDIA ERYTHRENA was at one time much in vogue in the United States as a sleep producer and to check cough, but it was recently discovered that its active principle had no narcotic effect and in large doses acted much like physostigmine.

SUMMARY OF THE GROUP ACTION.—*Depression of the sense of pain before complete narcotic action occurs. Great depression of the respiratory centre causing even a measurable decreased breathing capacity in small medicinal doses. A tendency to increased irritability of the cord. Easy acquisition of habit. Increasing power of oxidation by constant ingestion. Decrease in the movements of the stomach and intestines and also decrease in the secretion of all glands except sweat. Excretion by the stomach and intestines.*

THERAPEUTIC APPLICATION.—On account of the depressant effect upon the cerebrum, **morphine,** its derivatives and substitutes, are used to *arrest pain* and to *produce sleep*, when sleeplessness is due to pain, and to quiet other sensory irritations such as *cough*. It frequently gives much relief in *asthmatic attacks*. Morphine is used in cases of *diarrhœas* to decrease the peristalsis and the secretions of the intestines. It is also used to stop the movements of the gastro-intestinal tract in cases of inflammations, such as *gastritis*, *enteritis* and *peritonitis*, also in cases of *hemorrhage from ulcers of the stomach or intestines*, and lastly in *lead poisoning* to relieve the intestinal spasm. For these conditions, crude preparations of opium are preferable on account of their slower absorption and, therefore, more prolonged action. Because of its dilating influence upon the peripheral blood vessels, morphine is at times used, especially in the form of Dover's Powders, *to induce sweating*.

When dyspnœa is due to pleurisy, pericarditis or endocarditis, and accompanied by much nervousness, opiates may prove of great value.

Morphine and other preparations powerfully depressing respiration *should be used only with great care in diseases attended with a decrease in the respiratory capacity, as pneumonia. This drug should not be given for a long period of time in chronic curable or not rapidly fatal diseases*, in order to avoid the formation of

habit. **Codeine** is used almost exclusively to allay *cough* in such diseases as pulmonary tuberculosis or bronchitis. In such cases it is often preferable to morphine because it does not decrease bronchial secretion nor cause as much constipation. It cannot be used to influence severe pain on account of its weak action. It has been employed in *diabetes* where it probably acts favorably, if at all, by quieting the anxiety of the patient and by aiding him to bear better the restricted diet. **Heroin, Dionin** and **Peronin** have been used for the same conditions as codeine. Heroin should be given with great care on account of the depression of respiration and tendency to collapse which it causes. Crude preparations of **Cannabis Indica** are very unreliable, as also some of the pure principles on the market. It is sometimes employed to relieve pain and produce sleep when opium is contraindicated. **Pellotin,** has been used to relieve insomnia, but its use has been occasionally attended by disagreeable symptoms.

MATERIA MEDICA.

Opium (U.S.P., B.P.), inspissated, milky exudation obtained by incising the unripe capsules of the opium poppy (papaver somniferum). It is a brown resinous mass containing in the (U.S.P.) 9 per cent. and in the (B.P.) much less morphine besides a large number of other alkaloids including Codeine, Papaverine, Narcotine, Narcein and Thebaine. **Dose:**—Br. (½–2 grains). Average (U.S.P.) **0.1 G.**

Opii Pulvis (U.S.P.) containing about 12 per cent. morphine. **Dose:**—0.05–0.15 G.; not more than 0.5 in 24 hours. Average (U.S.P.) **0.065 G.**

Extractum Opii (U.S.P.,B.P.), containing 20 per cent. morphine. **Dose:**—0.01–0.05 G. Br. (⅕–1 grain). Average (U.S.P.) **0.03 G.**

Pulvis Ipecacuanhæ et Opii (U.S.P.), and Pulveris Ipecacuanhæ Compositus (B.P.), or Dover's Powder containing 10 per cent. each of powdered opium and ipecac. **Dose:**—0.3–0.5 G. Br. (5–10 grains). Average (U.S.P.) **0.5 G.**

Tinctura Opii (U.S.P., B.P.) or Laudanum containing in (U.S.P.) 10 per cent. and in (B.P.) much less opium. **Dose:**—0.5–1.5 c.c. Br. (10–30 ♏). Average (U.S.P.) **0.5 c.c.**

Vinum Opii (U.S.P.). **Dose:**—0.5–1.5 c.c. Average (U.S.P.) **0.5 c.c.**

Tinctura Opii Camphorata (U.S.P.) and Tinctura Camphoræ Compositæ (B.P.) Paregoric contains 0.4 per cent. opium. **Dose:**—5.0–15.0 c.c. Br. (1–3 ʒ). Average (U.S.P.) **8 c.c.**

Morphina (U.S.P.), white crystalline alkaloid, with a bitter taste, almost insoluble in water, slightly soluble in alcohol. It forms crystalline salts with acids, including sulphuric, acetic and hydrochloric acids. These salts, Morphinæ Sulphas (U.S.P.), Morphinæ Acetas (U.S.P., B.P.), Morphinæ Hydrochloridum (U.S.P., B.P.), are all soluble in water but difficultly soluble

in alcohol. **Dose:**—Of morphine and its salts, 0.002–0.03 G. Br. ($\frac{1}{10}$–$\frac{1}{2}$ grain). Average (U.S.P.) for morphine **0.01 G.** Average (U.S.P.) for morphine salts **0.015 G.**

Codeina (U.S.P., B.P.) or methylmorphine, white crystalline body, slightly soluble in H_2O, easily soluble in alcohol. **Dose:**—0.01–0.03. Br. ($\frac{1}{4}$–1 grain). Its sulphate and phosphate are more easily soluble in H_2O and are given in the same dose. Average (U.S.P.) **0.03 G.**

Dimethylmorphine, or dionin, artificial derivative of morphine. **Dose:**—**0.015 G.**

Diacetylmorphine, or heroin, another derivative of morphine. **Dose:**—0.005 G.

Benzylmorphine or peronin. **Dose:**—0.01–0.03 G.

Cannabis Indica (U.S.P., B.P.), flowering tops of cannabis sativa, Indian hemp, a plant growing in Hindustan and used by the natives as an intoxicant under the name of Haschisch or Gunjah. It contains the resin cannabinon or cannabinol, having narcotic properties, besides the alkaloid tetanocannabine which has an action similar to strychnine. The latter is present in such comparatively small quantities that the action of the crude drug is not influenced by it. **Dose:**—Br. ($\frac{1}{2}$–1 grain). Average (U.S.P.) **0.065 G.**

Fluidextractum Cannabis Indicæ (U.S.P.). **Dose:**—0.1–0.3 c.c. Average (U.S.P.) **0.05 G.**

Pellotina, alkaloid found in a Mexican cactus, Anhalonium Lewinii which is prepared by the natives in the form of an intoxicant beverage called Mescale. **Dose:**—0.01–0.05 G.

Lactucarium (U.S.P.), concrete, milky exudate of Lactuca Virosa or lettuce. No active principle has ever been extracted. **Dose:**—Average (U.S.P.) **1 G.**

GROUP OF AMMONIA.

AMMONIA and salts of ammonium, possess severe **irritant properties** depending chiefly upon their ease of diffusibility and basic nature. On account of this irritant action, *redness and blisters may result from application to the skin* and *deep inflammation and abscesses may occur after subcutaneous injection. Nausea and vomiting may take place after too copious internal administration.* Inflammation and spasm of the glottis, with death from asphyxia, frequently follows the inhalation of large quantities of ammonia gas. When smaller quantities have been inhaled, death may occur only in several days from capillary bronchitis. This local irritant action, when of a mild degree, may reflexly stimulate respiration and circulation.

Intravenous or subcutaneous injections of ammonium compounds produce a direct stimulation of the **central nervous system.** On account of the stimulation of the medulla, *a rise*

in blood pressure and an increase in the force of respiration occurs. The great rise of blood pressure and quickening of the pulse, immediately after an intravenous injection, is due to direct stimulation of the **heart,** but the moderate elevation which persists, is due to a stimulant action on the medullary centres. Stimulation of the **cord** produces an *increase in reflex irritability* leading in sufficient doses to *tetanic convulsions*. When the dose has been moderate, these symptoms pass away and the animal recovers, but when very large quantities are administered, paralysis of the medullary centres results and death occurs in general coma. In frogs, the irritant action upon the cord is often masked by the *paralyzing effect upon the motor end plates*. This action, although more marked in frogs, may even be present in warm blooded animals after the administration of ammonium bases of the fatty acid series.

None of the general actions of ammonia or the simpler ammonium compounds are noticed after administration by the alimentary tract, because their excretion is so much faster than their absorption by this channel, that never enough of the drugs are present at one time in the blood to produce an effect.

Ammonium and its simple salts with organic acids are *transformed by the liver of birds and reptiles into uric acid, and by that of mammals into urea*. Both of these are **excreted** by the urine. When salts of ammonium with strong mineral acids, such as ammonium chloride are administered, the increase of urea in the urine is not so great because some of the ammonia must remain combined with the acid in order to protect the body from acid intoxication. In the case of ammonium chloride, a part of the chlorine is excreted by the stomach as hydrochloric acid. On account of their transformation in the body before excretion, ammonium compounds do not affect the reaction of the urine. Some ammonia appears in the **sweat** and **bronchial secretion** when large doses of the same or its salts are injected subcutaneously or intravenously. Like all alkalies, they dissolve the mucous secretions with which they come in contact, either in the stomach or bronchi.

The different ammonium bases, as **Trimethylamin** and **Cholin,** have more or less the general action of ammonia, but the ultimate depressant effect and the curare-like action on the motor end plates is more in evidence.

Summary of the Group Action.—*Powerful local irritation leading to reflex stimulation of respiration and circulation. Only by subcutaneous or intravenous administration, is observed, a marked stimulation of medulla, cord and heart, giving rise to increased circulation, respiration and tetanic convulsions. In cold blooded animals paralysis of the motor end plates. Transformed by the liver of mammals to urea, by that of birds to uric acid and excreted chiefly by the kidneys.*

THERAPEUTIC APPLICATION.—Ammonia and salts of ammonium are sometimes given subcutaneously or intravenously in cases of *collapse* for their *stimulant action on the central nervous system.* They are more often given internally in the form of aromatic spirits of ammonia, or inhaled as smelling salts. By this form of administration, the stimulation is only of a reflex character and is consequently very transient.

On account of its local irritant action, ammonia is used in the form of liniments as a *counterirritant* over painful points. Salts of ammonium are employed in *bronchitis* to stimulate and ease expectoration. The frequent use of ammonia internally and externally for snake bites has no rational support.

MATERIA MEDICA.

Aqua Ammoniæ Fortior (U.S.P.), a solution of ammonia in water containing 28 per cent. of the gas by weight.

Liquor Ammoniæ Fortis (B.P.) 32½ per cent. by weight.

Aqua Ammoniæ (U.S.P.) and Liquor Ammoniæ (B.P.), a 10 per cent. ammonia solution in water.

Spiritus Ammoniæ Aromaticus (U.S.P., B.P.) or Spirit of Hartshorn, contains ammonia, ammonium carbonates, volatile oils and alcohol. **Dose:**—1.0 to 4.0 c.c. Br. (15–60 ♏). Average (U.S.P.), **2.0 c.c.**

Linimentum Ammoniæ (U.S.P., B.P.), contains about 3½ per cent. ammonia.

Ammonii Carbonas (U.S.P., B.P.) consisting of a mixture of the carbonate, bicarbonate and carbamate of ammonium is a translucent crystalline mass. Very soluble in water and emits the odor of ammonia. **Dose:**—0.2 to 0.5 G., Br. (3–10 grains). Average (U.S.P.) **0.25 G.**

Ammonii Chloridum (U.S.P., B.P.), white crystalline powder, with a cooling saline taste, freely soluble in water and in 50 parts of alcohol. **Dose:** —0.2–0.5. Br. (3–10 grains). Average (U.S.P.), **0.5 G.**

GROUP OF STRYCHNINE.

The typical drug of this group is the alkaloid Strychnine, obtained from the seeds of Strychnos Nux Vomica, and Ignatia. Others are Brucine, also from Strychnos, Calabarine from Calabar Bean, Gelsemine from Yellow Jasmine, Tetano-Cannabine from India Hemp, and Thębaine from Opium. Their similarity of action consists of an increase of the reflex activity of the cord, leading, in sufficient doses, to tetanic convulsions, which throws the body into opisthotonos.

When large doses of **STRYCHNINE** have been taken by a man, there appears in a very short time, *violent tetanic convulsions*, which grow rapidly in intensity and duration, until there is a fixation of the diaphragm in inspiration and death, due to asphyxia with consciousness remaining until just before the end. If the dose has not been so large, the convulsions may be repeated for many hours, elicited and intensified by the least external stimulation, such as a breath of wind, or the jar of a door, and under these conditions, death may take place from exhaustion. If the dose is still smaller, there may be only a stiffness of the neck, general muscular twitching, and convulsions which are only produced by external stimulation. Recovery takes place, leaving the subject exhausted and aching all over. That the convulsions are due to stimulation of the **cord,** may be proved by decapitation of a frog poisoned by strychnine, which will show symptoms as marked as if the cerebrum and medulla were intact. Yet, there is no doubt that the brain and medulla are also stimulated because their functions are intensified.

On account of the stimulation of the medullary centres there is an increase in the strength of **respiration** and a rise of blood pressure. This rise is not entirely due to the effect upon the **vasomotor centre,** but is also, in part, the result of a direct action on the vessel walls. There is a great stimulation of the

special senses; for the field of vision, the acuteness of hearing and of smell, are all increased.

The *increase of vision* may first be observed in about three hours after the administration of strychnine, but it is most intense after five or six hours. Usually it lasts about one day, although it may be present several days. It is probably due to direct action on the retinal cells, as it is more marked if strychnine is injected subcutaneously in the neighborhood of the eye, and the effect is seen best on the one near where the injection has been made. *In man the stimulation of the special senses and the medulla precedes that of the cord* so that increased reflexes and convulsions do not occur while these functions are much increased, if the dose is not too large.

Strychnine does not stimulate the **heart muscle,** but slows the rhythm of this organ by stimulation of the **vagus.** In cold-blooded animals as the green frog, it produces after a time, a paralysis of the **motor nerve endings,** just as curare. Occasionally, man and other warm-blooded animals show the paralytic action on the motor end plates and also *paralysis of the central nervous system.* These effects can only be seen in this class of animal when death does not take place early from spasm of the respiratory muscles. The paralysis of the central nervous system is quite frequently observed in rabbits.

The **habit** for strychnine is never formed when fairly good doses are given, as the susceptibility does not decrease but rather increases by cumulation, due to slow excretion. Occasionally, however, when minute doses are given and very slowly increased, a considerable degree of tolerance may be reached in some subjects.

The **treatment of acute poisoning** consists of arresting the convulsions with ether, chloroform or chloral, then removing the poison from the stomach by washing. The volatile anæsthetics are preferable, because if the paralytic symptoms of strychnine supervene, they can be more quickly removed and stimulants of the central nervous system administered. There is practically no hope of recovery when symptoms of paralysis have occurred, because the drug is so slowly excreted.

Strychnine increases the general **metabolism,** and, therefore, the heat production. It also increases the heat dissipation so that no rise of **temperature** is seen, but even a fall, just as after other convulsive agents. It is **excreted** very slowly by the kidneys, and because of this slow excretion small amounts may become stored up in the body until they have accumulated to a poisonous dose. For this reason, the therapeutic administration of strychnine for any length of time should always be interrupted for a period when none is given, in order to allow sufficient time for excretion.

Like most other alkaloids, it has a **local irritant action,** which shows itself when given internally, by an *improvement of the appetite,* an *increase in the digestive juices* and in the movements of the stomach and intestines. Sufficiently large doses may cause nausea, vomiting and diarrhœa.

The other alkaloids, **Brucine, Gelsemine** and **Thebaine** are much weaker than strychnine. Brucine and thebaine are more apt to show earlier symptoms of depression of the central nervous system.

SUMMARY OF THE GROUP ACTION.—*Great increase in the reflex irritability of the cord leading to tetanic convulsions. Earlier, and with small doses, stimulation of the medullary centres with increase in the respiration and circulation. Stimulation of the special senses, of sight, hearing, smell, taste and touch. When death is not produced by fixation of the diaphragm with very large doses, paralysis of the central nervous system and in cold-blooded animals, of the motor end plates. Slowing of the heart by stimulation of the vagus centrally, but no stimulation of the heart muscle. No habit formation, but cumulative effects on account of slow excretion which takes place by the kidneys.*

THERAPEUTIC APPLICATION.—The bitter taste and local stimulant action of **strychnine** are used in medicine to improve the *appetite,* increase the secretions of digestive juices and the absorption of food in *malnutrition* from *chronic diseases* or in the convalescence from acute sickness. For this purpose, the crude preparations of nux vomica are more suitable than the crystalline

alkaloid, because they are less readily absorbed and remain for a longer time in contact with the gastro-intestinal tract. Strychnine is used to improve the respiration and to raise the blood pressure in **collapse** from injuries, or from the action of the **narcotic poisons,** as in chloral poisoning or during ether or chloroform anæsthesia. It is employed in the treatment of different forms of pareses and paralyses; such as those occurring in neuritis due to lead or alcohol, or in injuries or diseases of the cord or in cerebral hemorrhage. *The best results are obtained in partial paralysis, especially of the sphincters of the bladder or anus when all the nerve fibres are not degenerated, and also, when an inflammatory stage is passed,* for it may increase the irritation of nerve tissues. It is to be *avoided in fresh hemorrhage from the brain,* as by increasing the blood pressure it might increase the bleeding.

It is often useful in *optic atrophy* and is best injected in the temple in the neighborhood of the affected eye every two or three days. It may prolong vision in slow running cases, for a period of a few years, by keeping the healthy optic fibres stimulated to increased perception. Naturally, in these cases it is in no sense a cure, as the vision is as poor as ever when its use is discontinued.

MATERIA MEDICA.

Nux Vomica (U.S.P., B.P.), seeds of Strychnos Nux Vomica, a tree growing in India and Malay Peninsula. They should contain 1.25% strychnine. **Dose:**—Average (U.S.P.) **0.065 G.** Br. (1–4 grains).

Extractum Nucis Vomicæ (U.S.P., B.P.). **Dose:**—0.01–0.05 G. Br. (¼–1 grain). Average (U.S.P.) **0.015 G.**

Fluidextractum Nucis Vomicæ (U.S.P.). **Dose:**—0.05–0.25 c.c. Average (U.S.P.) **0.05 c.c.**

Tinctura Nucis Vomicæ (U.S.P., B.P.). **Dose:**—0.3–1.0 c.c. Br. (5–15 ♏). Average (U.S.P.) **0.6 c.c.**

Strychnina (U.S.P.,B.P.), white crystalline, alkaloid, very insoluble in water, slightly soluble in alcohol, soluble in ether and chloroform. It forms salts with acids. It is intensely bitter so that its taste may be detected in the dilution of 1 to 700,000. **Dose:**—0.001–0.01 G. up to 0.02 G., in 24 hours; 0.03 G. has proved fatal. Average (U.S.P.) **0.001 G.** (Br. $\frac{1}{30}$–$\frac{1}{15}$ grain.)

Strychninæ Sulphas (U.S.P.), white crystalline, soluble in 50 parts of water, less soluble in alcohol. **Dose:**—0.001 to 0.01 up to 0.02 G., in 24 hours. **Dose:**—Average (U.S.P.) **0.001.**

Strychninæ Hydrochloridum (B.P.). **Dose:**—(Br. $\frac{1}{60}$–$\frac{1}{15}$ grain).

GROUP OF PICROTOXIN.

The most important substances which compose this group are Picrotoxin, the fish poison, Digitaliresin and Toxiresin from Digitalis, Samandarin from Salamanders, Coriamyrtin, Cicutoxin and Oleandresin.

PICROTOXIN shows its typical action in the form of *clonic convulsions*, due to stimulation of the **medulla,** and thus differs from strychnine which produces tetanic attacks by stimulating the cord. The stimulation of the centres in the medulla also produces *deep and even convulsive respirations*, a *rise of blood pressure*, a *slowing of the pulse*, *vomiting* and *salivation*. It is said that the cord is also stimulated and that the reflex irritability is increased, yet this action is insignificant compared to that on the medulla, as the convulsions are typically clonic and do not appear in a characteristic form in frogs after destruction of the medulla.

The **heart** itself is but little affected by picrotoxin, for the slowing of the pulse is due to stimulation of the vagus centre in the medulla, and although the heart is stopped in diastole in frogs, the standstill may be relieved by section of the vagus. The increase in blood pressure is exclusively the result of stimulation of the vasomotor centre.

The **respiration** is at first markedly stimulated through its centre, then it becomes convulsive, and lastly slowed and labored, due to ultimate central paralysis.

The use of picrotoxin for catching fish depends upon a spasm-like contraction of the outlet to their air bladders. These distended air sacs act like balloons and buoy up the animal so that he cannot get under water, then he may easily be gathered in nets. Almost the same condition is observed in frogs whose lungs become greatly distended with air on account of a spasmodic closure of the glottis.

The mother substance of **CICUTOXIN** or Cicuta Virosa, has given rise to cases of poisoning by being confounded with flavoring herbs, or eaten by children. The toxic symptoms are vomiting, pain in the abdomen, muscular tremor, convulsions of an epilep-

tiform character, quickened and labored respiration, unconsciousness and death.

SAMANDARIN, the poison obtained from the skin of salamanders, gives rise to symptoms in dogs which closely resemble hydrophobia and consist of great salivation, increased mucous secretion, convulsive respirations with a mixture of clonic and tonic convulsions, and lastly death through general paralysis. It produces a small rise of blood pressure and a slowing of the pulse. All these symptoms closely resemble those elicited by picrotoxin and are the result of stimulation of the medulla, also to a minor degree of the cord.

SUMMARY OF GROUP ACTION.—*Stimulation of the medullary centres producing an increase in the respiration and blood pressure, a slowing of the pulse, vomiting and convulsions of a clonic or epileptiform character.*

THERAPEUTIC APPLICATION.—**Picrotoxin** has been recommended as a *respiratory stimulant*, but its other and undesirable actions are too prominent to warrant this as a regular application. It was recommended by one authority to arrest the night sweats of phthisis and of other exhaustive diseases, on the theory that the latter were due to improper respiratory functions which might be improved by picrotoxin. It has also been used in the form of an ointment to destroy pediculi on the body.

MATERIA MEDICA.

Picrotoxinum (B.P.), a neutral principle, soluble in alcohol and only slightly in water, obtained from Anamirta Panniculata which is used extensively in India as a fish poison. **Dose:**—0.001–0.003 G. Br. ($\frac{1}{60}$–$\frac{1}{20}$ grain).

GROUP OF CAMPHOR.

The main and most important action of **CAMPHOR** is the result of stimulation of the nervous system, and especially of the centres in the medulla and brain. The constitutional action of this drug is slow to appear, on account of its difficult absorption, due to the fact that it is practically insoluble in the body fluids.

When a large dose is ingested by man, it produces at first, a

burning sensation in the stomach, and sometimes nausea and vomiting. This stimulation of the gastro-intestinal tract is followed by a general sensation of warmth, headache, mental confusion and excitement, and an increase in the force of the pulse, with a slowing in its rate.

In warm-blooded animals, camphor stimulates the centres of the medulla. On account of the stimulation of the **respiratory centre,** the amplitude and frequency of the *respirations may be considerably increased.* The action on the **vasomotor centre** brings about a *rise in the blood pressure.* This rise is not exclusively due to the effect on the centre, but is in great part the result of a direct stimulation of the **heart muscle,** as from the action of physostigmine. The *epileptiform convulsions,* sometimes observed after the administration of camphor in mammals, recur at varying intervals, and last from five to ten minutes. Usually after a few hours they cease and the animal recovers completely. These convulsions are probably due to a stimulant effect on the **cerebral cortex,** because, after the removal of the latter they do not occur. A slight degree of narcosis is sometimes observed in mammals, but the stimulant effect is usually paramount.

In the lower forms, such as frogs, moth, insects, moles and bacteria, camphor exerts a purely depressant action. Frogs become paralyzed exactly the same as from ether, and later these animals show a paralysis of the **motor nerve endings.** If the dose has been small they recover, if large, they die from general paralysis. On account of its depressant action on the lower vegetable forms, camphor is a disinfectant.

It lowers the body **temperature** when pathologically increased. Locally, it produces a severe irritant effect which is followed by a feeling of cold and anæsthesia. This **local irritant action** makes itself evident by severe pain at the point of application when camphor is given subcutaneously, and by irritation of the stomach and vomiting when it is given by the mouth. It is partially *oxidized in the body to camphoral,* but it is **excreted** by the urine as camphoglycuronic acid.

The other **STEAROPTENES** (camphor-like bodies), Borneol, Camphoroxim, Camphor monobromate, Menthol and Thymol, have to some extent the action of camphor, but they do not stimulate the heart and they ultimately depress the central nervous system. They paralyze more markedly the motor nerve endings in frogs. **Menthol** has an especially strong depressant action on the *sensory nerve endings*, and therefore, is a good analgesic. **Thymol** has very strong *antiseptic and antiparasitic action*, and its toxic effects are particularly marked on the hookworm.

Camphoric Acid is mentioned by most authors as having the same effect on the nervous system as camphor, but in addition, as producing a paralysis of the nerves supplying the *sweat glands* just like atropine. This opinion is entirely wrong, as camphoric acid is almost devoid of action. Eight grammes may be given subcutaneously in the form of sodium salts to a rabbit, without eliciting any symptoms. Such quantities injected into a vein, cause no action upon either the respiration or circulation. *Camphoric acid fails to show the slightest effect upon the secretion of sweat* even in the most careful experiments.

SUMMARY OF THE GROUP ACTION.—*Intense stimulation of the respiratory and vasomotor centres in the medulla, and increase in force of the heart muscle with resulting augmentation of the respiration and circulation. Later, stimulation of the cortex in higher animals with resulting clonic convulsions. Sometimes, in warm-blooded animals depression of the cerebrum with sleep following, but in very low organisms depression of the entire nervous system is almost the only action. Local irritation followed by local anæsthesia. Excretion through the kidneys, after combining with glycuronic acid.*

THERAPEUTIC APPLICATION.—Camphor is used in cases of *collapse*, on account of its stimulant effect upon the respiratory centre and upon the heart. This use is not always attended by success, because of the irregular and slow absorption of camphor even after subcutaneous administration. Besides this latter method is not very practical, due to its severe local irritant properties. It is used as an analgesic wash in *skin diseases* to

allay itching, also over wounds and ulcers as an *antiseptic*. For *local analgesic effect* **Menthol** is especially applicable, and has been used in the form of a stick rubbed over the temple and face for *neuralgia*. **Camphoric acid** is used to decrease sweat, especially in Phthisis, but without reason. **Camphor monobromate** is used as a sedative in conditions of nervous excitement and to decrease sexual irritability.

MATERIA MEDICA.

Camphora (U.S.P., B.P.) a stearoptene, obtained by the sublimation of cinnamomum camphora, a tree growing in China and Japan. It is a white crystalline body with burning, bitter taste and characteristic odor, and is soluble in alcohol, ether, chloroform and oils, only very sparingly in water. It liquefies when rubbed with thymol, phenol, menthol and chloral. **Dose:**—0.1–0.2 G. up to 1.0 G., in 24 hours. Br. (2–20 grains). Average (U.S.P.) **0.125 G.**

Aquæ Camphoræ (U.S.P., B.P.). **Dose:**—5.0–10.0. Br. (1–2 fl. ʒ). Average (U.S.P.) **8.0 c.c.**

Spiritus Camphoræ (U.S.P., B.P.) 10 per cent. **Dose:**—1.0–2.0 Br. (15–30 ♏). Average (U.S.P.) **1.0.**

Linimentum Camphoræ (U.S.P.).

Camphora Monobromata (U.S.P.) is a bromine substitute of camphor with almost the same solubility. **Dose:**—0.1–0.2. Average (U.S.P.) **0.125 G.**

Acidum Camphoricum (U.S.P.), oxidation product of camphor, soluble in alcohol and slightly so in hot water. **Dose:**—0.5–2.0 c.c. Average (U.S.P.) **1.0 G.**

Menthol (U.S.P., B.P.) a secondary alcohol from Oleum Menthæ Piperitæ. It is a white crystalline body with aromatic odor and burning taste: slightly soluble in water, but easily soluble in alcohol, ether and oils. It liquefies when rubbed with camphor, thymol, and chloral. **Dose:**—0.05–0.1. Br. (1–2 grains). Average (U.S.P.) **0.065 G.**

Thymol described under the Group of Phenol.

GROUP OF CAFFEINE.

This group consists of a number of chemically related substances extracted from plants of various families, which have been used for centuries as subsidiary articles of diet in different countries. The chief member, the alkaloid caffeine, is present in the coffee bean, in the Chinese tea leaves, in the cocoa bean, in matè or Paraguay tea, in Apalachian tea, in the kola nut of Central Africa, and lastly in guarana, a beverage prepared in Brazil from Paulinia fruits. Other members of the group allied to

caffeine, both chemically and pharmacologically, are theobromine found in the kola nut and cocoa bean, theophylline found in tea leaves, and different xanthin bases found in the urine of animals.

CAFFEINE stimulates the entire **central nervous system,** and thereby produces in man, in small doses, an *increased capacity for mental work,* in larger doses, dizziness, headache, ringing in the ears, restlessness, sleeplessness and even delirium. In the lower animals, it *increases the reflex irritability* of the cord very markedly, and produces, in sufficient doses, *convulsions* of either clonic or tetanic character. It stimulates the **vasomotor centres** in the medulla, and causes a rise of blood pressure. It also increases the functional activity of the **respiratory centre.** In dogs and cats, caffeine usually causes at first, vomiting and defecation, then tetanic convulsions, and lastly, death due to paralysis of the central nervous system and heart.

When this drug is injected directly into a **muscle** or into the artery going to a muscle, the latter becomes opaque, white and hard, as in rigor mortis. If the quantity applied is very small, only an *increase in the force of contraction* and in the capacity for work is noticed. This action partly explains the well known beneficial effect of caffeine upon men performing strenuous physical exercise, as long marches.

The muscles of the **heart** are stimulated, thus producing an increase in the force and usually in the rate of contraction. Occasionally the pulse rate is decreased, probably by stimulation of the vagus centre in the medulla. The value of the action on the heart is much decreased by the great irregularity of rhythm, which caffeine often produces. If the drug is injected intravenously, in large quantities, dogs, cats, and rabbits die from cardiac paralysis.

The increased **micturition** which is seen in man after the ingestion of caffeine, has also been observed in experimental animals, in which the secretion of **urine** may be increased several hundred per cent. above the normal. This diuretic action is not due to the increase in blood pressure alone, but is the result of a

direct stimulation of the secreting parenchyma of the kidney, and is always accompanied by a dilatation of the smaller blood vessels of this organ. The height of the diuresis varies in direct proportion to the dilatation of the renal smaller vessels, and at times, no diuretic action takes place when the blood supply of the kidneys is decreased by stimulation of the central nervous system, until the contracted vessels are dilated by some drug, as chloral. The urine contains only a small percentage of the caffeine ingested, but a considerable increase of the other xanthin bases, which are undoubtedly derived from it.

Caffeine does not increase nitrogenous **metabolism,** but may cause a greater excretion of carbon dioxide on account of the augmented muscular work which may be performed under this drug. It may raise slightly the body **temperature.** Chronic poisoning occurs in animals when caffeine is introduced by any of the channels of absorption. The gastro-intestinal tract suffers much, even if the drug is administered subcutaneously. Animals exhibit vomiting and diarrhœa and at autopsy marked inflammation of the stomach usually acompanied by ecchymoses. Much emaciation usually occurs before death.

A cup of coffee or of tea which contains 0.1–0.2 G. of caffeine may be taken with meals by most individuals without poisonous effects. Large quantities of either, however, are liable to produce headaches, palpitation and mental confusion and when excessive quantities are used over a long period of time, nervousness, gastric and intestinal disturbances, and irregularity of the heart may be noticed.

THEOBROMINE has little effect on the heart and nervous system, but it acts on the muscles as intensely as caffeine. It is the **diuretic** par excellence because its *action is lasting and powerful*, and in doses sufficient for diuresis, does not affect other organs, except that it occasionally causes a little irritation of the gastro-intestinal tract. Theobromine has a **diuretic action** more constant than that of caffeine because it never contracts the smaller renal vessels centrally, but always produces a marked dilatation. This dilatation is said to be of value in renal affections, by im-

proving the circulation of the kidney. The total albumen in the urine of patients with Bright's Disease has been found less under theobromine.

THEOPHYLLIN acts upon the central nervous system very much like caffeine. It has less action upon the heart, but is more apt to produce gastro-intestinal disturbances. Its diuretic effect is tremendous momentarily but of very short duration.

SUMMARY OF THE GROUP ACTION.—*Intense stimulation of the central nervous system, especially of the brain and medulla, giving rise to an increase in mental activity, also increase in the efficiency of the respiration and circulation. Stimulation of the cord which may lead to tetanic convulsions, best seen in the lower grade of animals. Stimulation of the renal functions by direct action on the kidneys. Increase in the force of contraction of the heart sometimes accompanied by irregularity of the pulse. Direct stimulation of the striated muscles leading to increased capacity for work, while with large amounts directly applied, permanent rigor with changes in the histological texture of the muscles.*

THERAPEUTIC APPLICATION.—Both **Caffeine** and **Theobromine** are used with good results on account of their diuretic action in cases of *heart and liver dropsy* to help the elimination of the accumulated fluid. The use of these substances in Bright's Disease, is sometimes attended with less beneficial results, because the renal epithelium may be destroyed to such an extent that it is incapable of being stimulated. In this latter condition they are also liable to increase the irritation. Theobromine is used in preference to caffeine as a diuretic, because it is more powerful, and because it does not stimulate the cord nor contract the vessels of the kidney.

Caffeine is given in cases of *narcotic poisoning* and collapse, because of its stimulant effect on the respiration and heart.

In *nervous exhaustion* it may be useful because of its general stimulant action upon the central nervous system. Its use in *migraine*, which is sometimes beneficial and sometimes harmful, cannot as yet be explained.

MATERIA MEDICA.

Caffeina (U.S.P., B.P.), is a mildly basic substance obtained from the tea leaves and coffee bean but is also present in many other plants. It is present to the extent of about 0.12 gram in a good cup of coffee made from 15 grams of coffee or in a cup of tea made from 5 grams of tea leaves. It is a white crystalline substance with bitter taste, difficultly soluble in water. It forms easily soluble double salts with sodium salicylate and sodium acetate. **Dose:**—0.2 G. per day up to 0.6. Br. (5 grains). Average (U.S.P.) **0.065 G.**

Caffeina Citrata (U.S.P.) and Caffeina Citras (B.P.), white powder, decomposed by warm water, soluble in three parts of water, composed of a loose combination of citric acid and with caffeine. **Dose:**—0.1–0.5 G. Br. (2–8 grains). Average (U.S.P.) **0.125 G.**

Caffeina Citrata Effervescens (U.S.P.) or Caffeinæ Citras Effervescens (B.P.), a mixture of sugar, sodium bicarbonate and citric acid containing 4 per cent. caffeine in the (U.S.P.) and 2 per cent. in the (B.P.). **Dose:**—1–10 G. Br. (15–150 grains). Average (U.S.P.) **4.0 G.**

Theobromina, crystalline powder, very difficultly soluble in water. **Dose:**—0.5 G.

Theobrominæ Sodio-Salicylas, or diuretin, is a white powder easily soluble in water and containing 50% theobromine. It changes color and gradually decomposes on standing. **Dose:**—1.0 G.

Theobrominæ Sodio-Acetas, or agurin, double compound of theobromine and sodium acetate; very soluble in water. **Dose:**—1.0 G.

Theobrominæ Sodio-Formas, or theophorin. **Dose:**—0.5 G.

Theophyllina, white, crystalline body, difficultly soluble in water. **Dose:**—0.2–0.4 G.

Fluidextractum Guarana. Dose:—3.0–8.0 c.c.

GROUP OF HYDROCYANIC ACID.

HYDROCYANIC ACID or Prussic acid is one of the most rapidly acting poisons. After a large dose has been taken by man or lower animals, they *may fall lifeless to the ground* in a few seconds without any premonitory symptoms, except, perhaps, a scream and a few convulsions.

When smaller doses of the acid or of its simple salts such as the cyanides of potassium, sodium and mercury are ingested, the subject begins to show an increase in the frequency of the respiration, also a rise of the blood pressure, with restlessness and muscular twitching. These symptoms are soon followed by clonic convulsions, unconsciousness, dilatation of the pupils, diminution in the force and frequency of respiration, and fall of blood pressure. The respirations become progressively fewer until death takes place by asphyxia.

Human beings who have taken a small poisonous dose, experience a burning, bitter taste, a numbness in the mouth and throat, an increase in the salivary secretion, then a feeling of oppression in the chest with pain over the heart and dyspnœic respirations. After an increase in these symptoms they die, as do the lower animals, with convulsions and loss of consciousness.

The symptoms are due to a primary stimulation of the **central nervous system** followed by paralysis of the same. Hence *the respiratory, vasomotor and vagus centres are first stimulated, then depressed.* The convulsive attacks are probably due to a stimulation of the centre of convulsion.

The **heart** is depressed chiefly through its motor ganglia, as its musculature remains irritable to electricity long after the organ has stopped beating. After moderately large doses, the respiratory centre is paralyzed before the heart, as resuscitation may sometimes be brought about by artificial respiration when breathing has practically ceased. Enormous quantities may arrest both the heart and respiration at the same time.

Hydrocyanic acid forms a loose combination with the oxyhæmoglobin of the **blood** and decreases its oxidative powers. Thus, the blood in the veins may retain its oxygen and look bright red like that of the arteries. The formation of a loose compound with hæmoglobin in the living body is not of great significance in explaining the poisonous action of hydrocyanic acid because it produces the same toxic effect on animals without any hæmoglobin, and also in frogs whose blood has been replaced by salt solution. It yields a compound with methæmoglobin which has a bright cherry-red color. To this combination, is due the peculiar post-mortem appearance of the blood in dependent parts of victims of prussic acid poisoning.

The **metabolism** is much decreased by this drug, therefore, less oxygen is absorbed and less carbon dioxide excreted, than normally. This may be due to its general effect on protoplasm, for hydrocyanic acid can be considered in many respects a *general protoplasmic poison*, because it affects markedly the

functions of the lower organisms. It even stops the action of certain unorganized ferments.

Hydrocyanic acid and simple cyanides are **excreted,** to a certain extent, by the kidneys as sulpho compounds.

Locally applied, a solution of the acid depresses the endings of the **sensory nerves** and, therefore, decreases sensibility, but after internal administration, no such results are to be observed.

Some cases of **poisoning** occasionally occur in chemical laboratories, following the inhalation of the fumes of this terrific poison. Others result from suicidal attempts by scientific men, as chemists and doctors, who choose this drug on account of its rapid action. In presence of such cases, the chief method of treatment consists of *artificial respiration.* The poison is rapidly transformed in the body and when respiration is maintained recovery may take place if the dose has not been large enough to paralyze the heart. The best hope of success is in cases of accidental inhalation of the gas, for after the suicidal ingestion, the dose is as a rule so overwhelming that nothing can be done.

SUMMARY OF THE GROUP ACTION.—*Intense depression of the different centres in the medulla especially that of respiration, after a brief stimulation. The motor ganglia of the heart paralyzed directly by a large dose. Stimulation of the convulsive centre. Formation of a loose compound with hæmoglobin which reduces its oxidative properties. Paralysis of all forms of protoplasm and even arrest of the action of some unorganized ferments. By local application, paralysis of the sensory nerve endings, with analgesic effect.*

THERAPEUTIC APPLICATION.—The use in medicine of **hydrocyanic acid** and its salts has properly become obsolete. They possess no desirable action, and considerable danger. The acid in 2 per cent. solution was formerly employed to check the *cough in phthisis* and to allay the pain in some affections of the *stomach.* Nowadays, we have much safer drugs for these purposes and only employ as *flavoring agents,* preparations of **wild cherry** and **bitter almonds** which contain traces of hydrocyanic acid.

MATERIA MEDICA.

Acidum Hydrocyanicum is a colorless liquid with the odor of bitter almonds. It forms simple salts with sodium, potassium, mercury and silver which are all decomposed in the body with the formation of free hydrocyanic acid and, therefore, have identical action with this acid. The double salts, ferro and ferri cyanides of sodium or potassium, are not decomposed in the body and, therefore, do not have the same action as hydrocyanic acid, but merely act as purgatives. The nitrocyanide of sodium is a double salt which by exception is decomposed in the body and has a typical cyanide action. Hydrocyanic acid occurs native in a number of plants. It is formed by the decomposition of Amygdalin, by dilute acids, or by a ferment Emulsin. Both Amygdalin and Emulsin are present in bitter almonds and wild cherry and in the seeds of other fruits, but the amount of hydrocyanic acid liberated is not, as a rule, sufficient to be poisonous.

Acidum Hydrocyanicum Dilutum (U.S.P.,B.P.), is a 2 per cent. solution of hydrocyanic acid. It is a colorless liquid with the characteristic odor. **Dose:**—0.1–0.5 c.c. Br. (2–8 ♏). Average (U.S.P.) **0.1 c.c.**

Prunus Virginiana, bark of wild cherry.

Fluidextractum Pruni Virginianæ (U.S.P.). **Dose:**—2.0–4.0 c.c. Average (U.S.P.) **2.0 c.c.**

Infusum Pruni Virginianæ (U.S.P.). **Dose:**—15.0–60.0 c.c. Average (U.S.P.) **60 c.c.**

Syrupus Pruni Virginianæ (U.S.P.). **Dose:**—5.0–15.0 c.c. Average (U.S.P.) **4.0 c.c.**

Amygdala Amara, kernels of bitter almonds.

Aqua Amygdalæ Amaræ (U.S.P.). **Dose:**—5.0–15.0 c.c. Average (U.S.P.) **4.0 c.c.**

Spiritus Amygdalæ Amaræ (U.S.P.). **Dose:**—1.0–2.0 c.c. Average (U.S.P.) **0.5 c.c.**

GROUP OF CARBON MONOXIDE.

This group contains only **CARBON MONOXIDE,** the chief toxic agent of illuminating gas. Unlike hydrocyanic acid, the *characteristic action is dependent upon its combination with the hæmoglobin of the blood* because it has no influence on animals without hæmoglobin and it does not seem to interfere with lower states of protoplasm.

If forms with **hæmoglobin** a very stable compound which cannot act as an oxygen carrier, therefore, when enough has entered the system, there occurs asphyxia of all the tissues. To this action, all the symptoms of poisoning are referable. The blood has a purplish-red hue which does not change when shaken with air, as does ordinary venous blood. The quantity of carbon monoxide combined with hæmoglobin does not seem to depend

upon the total quantity respired, but upon the partial pressure. When the quantity is very small, it remains dissolved in the plasma and does not combine with hæmoglobin. The combining power of carbon monoxide bears a certain relation to its concentration as expressed in the following table which has been prepared by Hüfner to show this proportion:

Percentage of carbon monoxide in air of respiration	Percentage of carbon monoxide hæmoglobin in blood.
0.01	6.83
0.025	15.5
0.1	42.0
0.5	78.65
1.0	86.0
2.0	93.72
3.0	95.0

When air containing from 0.02 to 0.024 per cent. of carbon monoxide is inhaled by man, no poisonous symptoms occur as long as that proportion is not increased. With concentrations of 0.4 to 0.5 per cent., i. e., when about 70 per cent. of the hæmoglobin has been combined with this gas, death takes place with stoppage of **respiration.**

Carbon monoxide is *not oxidized in the body.* It is gradually dissociated from the hæmoglobin, and travels dissolved in the plasma. It is **excreted** by the lungs. The separation of carbon monoxide from hæmoglobin is more rapid in dogs than in men. A dog made unconscious by carbon monoxide may recover within ten or fifteen minutes, while a man may remain in coma for hours.

The symptoms of poisoning in animals consist, at first, of quickening of the pulse and respiration, great restlessness, convulsive contraction of the head and limbs and at last well-marked convulsions and death. Glycosuria usually occurs and is probably due to interference with the respiratory processes.

In human beings, the **toxic symptoms** can be divided into three stages: in the first, there are headache, knocking in the head, roaring in the ears, dizziness, difficulty in breathing, palpitations, reddening of the face and mucous membranes, nausea and vomiting and loss of consciousness; in the second, there occurs a

series of clonic convulsions of greater or lesser intensity; in the third, general paralysis with relaxation of the sphincters of the bladder and anus, and very weak respiration and heart beat, until both cease.

When the subject is removed from the poisonous atmosphere and given fresh air, in the first stage, he invariably recovers; in the second stage, recovery is also frequent, but in the third stage, the patient usually dies. When recovery does take place in the third stage, it may be complete and immediate, or it may leave, for a considerable time, different *complications*, as paralysis of the limbs, of the sphincters, loss of speech, blindness and disturbances of cerebration.

The **treatment of poisoning** is self evident and consists of placing the patient in pure fresh air and administering artificial respiration. Lately blood transfusion has been advocated and found of service experimentally.

SUMMARY OF THE GROUP ACTION.—*The formation of a very difficultly decomposed compound with hæmoglobin which interferes with respiration and gradual death of the tissues. The symptoms divided into three stages: firstly, unpleasant sensations; secondly, convulsions from asphyxia; and thirdly, general paralysis and death.*

GROUP OF ATROPINE.

This group is composed of various alkaloids extracted chiefly from plants of the Solanacæ family. The principal ones are atropine, hyoscyamine and scopolamine. The different members of this group resemble atropine closely, both in chemical composition and in pharmacological action.

ATROPINE depresses the nerve terminations of secretory glands, of smooth muscle fibers, and of inhibitory apparatuses. On the central nervous system, it produces a stage of stimulation which is followed by one of depression.

The first **symptoms** observed in man consist of a sensation of dryness and irritation of the throat, thirst and difficulty in swallowing, all of which result from the decreased formation

of saliva and mucus. The skin becomes dry, hot and red. Nausea and vomiting may occur. The pupils dilate and the power of accommodation is lost. The pulse is full and rapid, due to a rise in blood pressure resulting from the stimulation of the vasomotor centre and from the paralysis of the inhibitory vagus. The subject is at first excited, delirious and maniacal. The stimulation of the brain which brings about these symptoms is soon replaced by depression, causing decreased consciousness and later deep coma.

Besides the **secretory nerves** of the sweat and salivary glands, those of the bronchi, stomach, intestines, pancreas, liver and mammæ are depressed, with a resulting decrease in the secretions of these organs. Both the total quantity of the gastric juice and also the percentage of hydrochloric acid is diminished.

The **inhibitory apparatuses** of the vagus and splanchnics are paralyzed, with a consequent increase in the rate of heart beat and in the peristalsis of the intestines. The movements of the latter are afterwards decreased by a paralysis of the motor nerve supply to their smooth muscle fibres, and with very large doses, by a paralysis of the muscles themselves.

Depression of the motor nerve endings of the **smooth muscle** fibres of the bladder, ureters, uterus, spleen and œsophagus, decreases the power of contraction of these organs. It is said that the sensory endings are also depressed.

The **pupils** are widely dilated and *accommodation and adaptation of the eye are both paralyzed* on account of the depression of the oculomotor nerve endings in the ciliary and iris muscles. This action is best seen after local application. The introduction of one drop of a 1 per cent. solution in the eye, dilates the pupil and paralyzes accommodation in about one and a half hours. Paralysis of accommodation may last four or five days, while dilatation of the pupil may be observed after one week. The intraocular pressure is raised, because the dilated iris obstructs the canal of Schlemm, which assists in the draining of the eyeball, and because the blood vessels in the eye are dilated.

Stimulation of the **cerebrum** shows itself by excitement and

delirium. The primary stimulation of the respiratory and vasomotor centre in the **medulla** brings about an *increase in the force of respirations and a rise of blood pressure.* Only the larger internal blood vessels are contracted, for those of the skin, surface of the brain, and of the eye, are dilated. Stimulation of the central nervous system is followed by depression. The latter causes unconsciousness, fall in blood pressure and death from respiratory failure. Large doses, applied locally to the **heart,** not only paralyze the vagus, but also the cardiac muscles themselves. At first, only a great increase in the rate of heart beat takes place, but later the force of the heart's contraction is decreased until complete arrest occurs.

Atropine produces a rise of **temperature,** probably through the heat regulating centres. It is in great measure **oxidized** in the body, although a smaller portion is **excreted** in the urine.

HYOSCYAMINE resembles atropine very closely in its action. It differs from the latter, as it usually *depresses the cerebrum* from the beginning and thus produces sleep, without an initial stage of excitement.

SCOPOLAMINE or hyoscine, acts very much like atropine, except that it is still more depressant to the cerebrum than hyoscyamine. Its narcotic effects are so marked that it has been used as a general anæsthetic.

HOMATROPINE has the same general action as atropine, but less intense. It dilates the pupil and relaxes accommodation more quickly than atropine, yet the paralysis of adaptation and accommodation is of shorter duration.

SUMMARY OF THE GROUP ACTION.—*Paralysis of the nerve endings of secretory glands, smooth muscle fibres and inhibitory apparatuses with decrease in the secretion of the skin, respiratory and gastro-intestinal tract, with relaxation of the smooth muscles in the gastro-intestinal and urinary tracts, also with relaxation of the iris and ciliary muscles giving rise to paralysis of accommodation and adaptation but increase in the intraocular tension. Quickening of the pulse due to paralysis of the vagus endings. The respiratory and vasomotor centres in the medulla first stimu-*

lated then depressed. The brain usually first stimulated, giving rise to delusional symptoms, then depressed with resulting narcosis.

THERAPEUTIC APPLICATION.—Atropine is used in small doses to increase the functional activity of the medulla in cases of *collapse*, or of poisoning, where either or both the respiratory and vasomotor centres are depressed. It is considered a good *antidote for morphine* on the centre of respiration.

On account of its action on secretory nerves, it is used to *decrease sweating in phthisis* or obesity, to decrease excessive secretions of the bronchi in *bronchorrhœa*, before etherization to lessen salivation, and to stop the *secretion of milk*.

It is used on account of its paralyzing action on the vagus in cases of *low pulse rate* due to intracranial tumors or tumors of the neck pressing on this nerve. It is also used to paralyze the vagus terminations in the lungs in order to relieve spasmodic contraction of the bronchiole, as is supposed to occur in *asthmatic attacks*.

It is useful in *spasmodic constipation*, as that due to *lead poisoning*. In such cases it acts by depressing the motor nerve endings of the smooth muscles and even the muscle fibres themselves, thus relieving the spasm.

It is used to relieve spasmodic contraction of other organs, such as that of the ureter, bladder, gall bladder, bile ducts and urethra, in cases of *stones* or other conditions in these organs producing spasm. On account of both its depressing effect on the secretion of hydrochloric acid and its paralyzing effect upon the pyloric sphincter, atropine has been used with much success, both internally and by subcutaneous injection, in *diseases of the stomach* attended with hyperacidity and pylorospasm, as ulcers and erosions.

Atropine finds a great field of usefulness in *ophthalmology*, where it is employed to dilate the pupil and to paralyze accommodation in order to permit of examination of the eye. The dilatation is also used to prevent anterior adhesions or to break them up when they exist. It is *contraindicated* where there is an increase of intraocular tension, as in *glaucoma*. It should only be used in small quantities in the eye, as systemic poisoning may

occur from absorption. Well-marked local irritation of the eye, which is of no serious import, may be seen after the application of atropine to this organ.

Atropine preparations are sometimes employed as a *local anodyne* over neuralgic nerves or rheumatic joints.

Hyoscyamine and **Scopolamine** are both used as *narcotics* in cases of *nervousness, delirium tremens, mania,* and other conditions attended with an increase in the functional activity of the cerebrum. Scopolamine is especially valuable for these conditions and has also been used as a general anæsthetic in combination with morphine.

Homatropine is used exclusively *in the eye* to dilate the pupil and relax accommodation during examinations. It is preferable to atropine for this purpose because the dilatation is more rapid and less lasting. Sometimes accommodation is not completely paralyzed by homatropine.

MATERIA MEDICA.

Belladonna Folia and **Belladonnæ Radix** (U.S.P., B.P.), leaves and roots of Atropa Belladonna or Deadly Nightshade, a bushy shrub growing in Europe and America. The leaves contain 0.35 G. while the roots contain 0.5 G. of total alkaloids. Among these are atropine, belladonnine, hyoscyamine, scopolamine, atroscine and atropamine. Atropine is present in largest quantities.

Tinctura Belladonnæ Foliorum (U.S.P.). Tinctura Belladonna (B.P.). **Dose**:—0.3–2.0. Br. (5–30 ♏). Average (U.S.P.) **0.5 c.c.**

Emplastrum Belladonnæ (U.S.P., B.P.).

Unguentum Belladonnæ (U.S.P., B.P.).

Extractum Belladonnæ Foliorum (U.S.P.). Extractum Belladonnæ Alcoholicum (B.P.). **Dose**:—0.005–0.05. Br. ($\frac{1}{10}$–1 grain). Average (U.S.P.) **0.01 G.**

Fluidextractum Belladonnæ Radicis (U.S.P.). **Dose**:—0.05–0.2. Average (U.S.P.) **0.05 c.c.**

Hyoscyamus (U.S.P.) or Hyoscyami Folia (B.P.), leaves and flowering tops of Hyoscyamus Niger or Henbane. It contains the alkaloids, scopolamine, hyoscyamine and atropine. The total alkaloids amount to 0.08%. The latter is present in smaller quantities than the other two.

Tinctura Hyoscyami (U.S.P., B.P.). **Dose**:—0.5–5.0 c.c. Br. (½ ʒ). Average (U.S.P.) **2.0 c.c.**

Fluidextractum Hyoscyami (U.S.P.). **Dose**:—0.3–1.0. Br. (5–15 ♏). Average (U.S.P.) **0.2 c.c.**

Stramonii Semen and **Stramonii Folia** (U.S.P., B.P.), seeds and leaves of Datura Stramonium or Jimpson Weed. These contain the alkaloid, hyoscyamine, atropine with smaller quantities of scopolamine.

Fluidextractum Stramonii (U.S.P.). **Dose:**—0.05–2.0. Average (U.S.P.) **0.05 c.c.**

Tinctura Stramonii (U.S.P.,B.P.). **Dose:**—0.5–1.5. Br. (17–20 ♏). Average (U.S.P.) **.0 c.c.**

Other plants containing the members of the atropine series are Duboisia Myoporoides, Scopolia Atropoides and Atropa Mondragora.

Atropina (U.S.P.,B.P.), white, crystalline alkaloid with a bitter taste, soluble in 3 parts alcohol, almost insoluble in water. It is an ester formed by the union of the base tropine and tropic acid. **Dose:**—0.0005–0.001. Br. ($\frac{1}{200}$–$\frac{1}{100}$ grain). Average (U.S.P.) **0.0004 G.**

Atropinæ Sulphas (U.S.P.,B.P.), white, crystalline, soluble in H_2O and alcohol. In the eye 1 per cent. solution. **Dose:**—0.0005–0.001. Br. ($\frac{1}{200}$–$\frac{1}{100}$ grain). Average (U.S.P.) **0.0004 G.**

Hyoscyamina, isomer of atropine. It has almost the same properties. **Dose:**—0.0005–0.001.

Hyoscyaminæ Sulphas (U.S.P.,B.P.), white crystalline deliquescent body, soluble in H_2O and alcohol. **Dose:**—0.0005–0.001. Br. ($\frac{1}{200}$–$\frac{1}{100}$ grain). Average (U.S.P.) **0.0005 G.**

Hyoscyaminæ Hydrobromidum (U.S.P.,B.P.), same properties as the sulphate, but not deliquescent. **Dose** same as above.

Hyoscinæ Hydrobromidum (U.S.P.,B.P.), colorless crystals soluble in H_2O and alcohol, slightly efflorescent. **Dose:**—0.0003–0.0005. Br. ($\frac{1}{200}$–$\frac{1}{100}$ grain). Average (U.S.P.) **0.0005 G.**

Scopolaminæ Hydrobromidum (U.S.P.). **Dose:**—Average (U.S.P.) **0.0005.**

Homatropinæ Hydrobromidum (U.S.P.,B.P.), an artificial alkaloid, being an ester of tropine and phenylglycolic acid, soluble in 6 parts of H_2O, used in the eye in 1 per cent. solution.

GROUP OF AGARIC ACID.

AGARIC ACID in the form of its crude preparation, the fungus, white agaric, has been used for two centuries in Europe to decrease the excessive secretion of sweat.

Like atropine, it paralyzes the nerve endings of the **sweat glands,** causing dryness of the skin. It does not paralyze the nerve terminations of the salivary glands, nor those of the gastro-intestinal tract, nor does it paralyze the nerve endings of organs with smooth muscle fibres, nor the inhibitory apparatus of the vagus.

It is a very powerful **local irritant** which may produce abscess by subcutaneous injection, nausea, vomiting and diarrhœa after internal administration, and sneezing after snuffing. Although the local irritation may be very severe after ingestion, this mode of application never produces fatal results. The crude drug, or

impure Agaricin, which contains very irritant resinous acids, cause much more irritation than the pure agaric acid.

When injected subcutaneously as a sodium salt in the dose of 0.01 G. into a small cat, the acid arrests the secretion of sweat on the plantar side of the paw within four to six hours and electrical stimulation of its sciatic nerve does not produce sweating. With larger doses, it produces at first a stimulation of the respiratory, vasomotor and vagus centres in the **medulla,** with a consequent increase in respiration and blood pressure and a slowing of the pulse. With still larger doses, paralysis, failure of respiration, circulation, and quickening in the rate of the pulse occur. In frogs, large doses paralyze the heart directly.

SUMMARY OF THE GROUP ACTION.—*Decrease in the secretion of sweat by paralysis of the nerve endings of the sudoriferous glands. At first stimulation of the respiratory and vasomotor centres in the medulla, followed by depression. Severe local irritant action leading to inflammation of the skin, vomiting and diarrhœa.*

THERAPEUTIC APPLICATION.—It is used almost exclusively as an antihydrotic to arrest the *night sweats* of *phthisis.* It requires about 0.02 to 0.03 G. to produce this effect. It may cause nausea in larger doses.

MATERIA MEDICA.

Agaricinum, obtained from the fungus Boletus Laricis, growing on European larch trees; it is a white powder, soluble with great difficulty in water and contains Agaric Acid with impurities, and is about one-twentieth as strong as the latter. **Dose:**—0.01–0.06 G.

Acidum Agaricum, white powder, a pure preparation obtained from the above, soluble with difficulty in water, but dissolves easily in the presence of alkalies with the formation of salts. **Dose:**—0.0005–0.003 G.

GROUP OF MUSCARINE AND PILOCARPINE.

This group comprises Muscarine, the poisonous principle of toadstools or fly-mushrooms; the two alkaloids, Pilocarpine and Pilocarpidine present in Jaborandi leaves; and Nicotine obtained from tobacco. The characteristic action of these alkaloids is diametrically opposite to that of atropine. They stimulate all the peripheral organs which are depressed by atropine, such as

the secretory glands, smooth muscle fibres and inhibitory apparatuses.

MUSCARINE by *stimulating the inhibitory vagus in the* **heart,** *slows and even stops the latter in diastole.* By increasing the function of **secretory nerve endings,** it brings forth an increase in the secretion of the salivary, laryngeal, sweat, gastric, intestinal and pancreatic glands. By stimulation of the nerves of the **smooth muscles** of the stomach and intestines, it produces contraction of these organs with vomiting and diarrhœa. On account of its effect on the nerves of the smooth muscles of the bladder, it causes a contraction of the latter and urination. The stimulant action on the endings of the nerves supplying the muscles of adaptation and accommodation, produces a *contraction of the pupil and a spasm of accommodation.* Even the muscles of the spleen, bronchi and uterus are contracted by muscarine, with consequent contraction of these organs. This alkaloid produces in cold-blooded animals, paralysis of the **motor end plates** of nerves of the skeletal muscles. This depressant action on motor nerve plates is more striking after the administration of artificial muscarine and various ammonium bases which have the general characteristics of the group.

In contrast with its stimulant action on the peripheral nervous system, muscarine exerts chiefly a depressant influence upon the **central nervous system.** After a preliminary stimulation of the respiratory centre, causing an increase in the rate and depth of respiration, it produces a depression which results in a *decrease of the respirations* followed by a total arrest. The vasomotor centre is also depressed, therefore *the blood pressure is lowered.* The other parts of the central nervous system are not so markedly affected.

In cases of **poisoning** in human beings, the first symptoms resulting from stimulation of the peripheral organs are salivation, sweating, nausea, vomiting, cramps and diarrhœa, contracted pupils. Usually at first there is increase in pulse rate from the nausea, followed by a decrease in its rate, due to a stimulation of the vagus nerve. Symptoms of central depression and collapse

follow closely the appearance of those of peripheral stimulation, and consist of dizziness, oppression, stupor and loss of consciousness. Death takes place from arrest of the heart.

Although the **pupils** are always contracted by pure muscarine, they are often dilated in poisoning by fly-mushrooms containing Muscaridine which acts like atropine.

PILOCARPINE resembles muscarine very closely in its action, but is much less powerful. The stimulant action on the peripheral organs and especially on those of **sweat** and salivation, forms the striking feature of the action of pilocarpine. With small doses in man, *profuse sweating often accompanied by salivation* are practically the only symptoms observed. With larger doses, contraction of the **smooth muscles** of the stomach and intestines, with nausea, vomiting and diarrhœa occurs. The **central nervous system** is affected later, and only with much larger doses than muscarine. It also differs from muscarine, by paralyzing the inhibitory apparatus of the **vagus** after the primary stimulation; thus it increases the pulse rate after a primary decrease. Later it paralyzes the **heart** itself. Pilocarpine also partly dilates the **pupils** after first contracting them, by a paralysis of the oculomotor nerve in the iris, following its stimulation. If it were not for the contraction of the pupils, the intraocular pressure would be raised by pilocarpine, therefore, it is only lowered when they are well contracted.

PILOCARPIDINE acts like pilocarpine, but less powerfully.

NICOTINE has much the same action as pilocarpine, but it depresses much more the **central nervous system,** and especially the respiratory centre. It causes clonic convulsions and fibrillary twitchings of different muscles which are due partly to primary stimulation of the central nervous system and of the **motor nerve endings,** and partly to the asphyxia caused by paralysis of the respirations.

As a result of this primary effect on the central nervous system, the respiration is increased and the blood pressure is raised. These evidences of stimulation soon subside when the blood pressure falls and *death takes place from respiratory paralysis.*

Nicotine stimulates at first the inhibitory, secretory and motor **peripheral nervous apparatus.** This is succeeded by a paralysis of these organs, so that the slowing of the heart, due to stimulation of the vagus, is soon replaced by quickening, due to paralysis of this nerve. The increased salivation, lachrymation and sweating are followed by a diminution of these secretions; the spasmodic contraction of the smooth muscles of the intestines is followed by relaxation. The **pupil** is at first contracted, but later partly dilated. The seat of action is not, as with muscarine and pilocarpine, the nerve endings, but is the ganglia between the nerves and the organs.

At first, nicotine stimulates the **cardiac muscles,** and this is in part the cause of the quickening of the pulse; this stimulation is soon followed by a depression and the pulse becomes weak with the paralysis of the heart muscle.

The increased blood pressure observed at the beginning of the action of nicotine is due, not only to the stimulation of the heart muscle, but also to a stimulant action on the **vasomotor centre** in the medulla and on the ganglia in the walls of the blood vessels.

In frogs, nicotine at first stimulates **motor nerve endings** and causes twitching, but later paralyzes them, as does curare.

When tobacco is first used by persons unaccustomed to its effect, a condition of **acute poisoning** of greater or lesser intensity occurs. In the milder cases there are only dizziness, quickened pulse, nausea, vomiting and diarrhœa. In severer types, convulsions, unconsciousness and even collapse may be observed after the first smoke.

Prolonged use of nicotine in the form of smoke, chew or snuff brings about a condition of tolerance so that much more can be taken without apparent disagreeable symptoms, and the habitual smoker can smoke with impunity quantities of tobacco which might produce collapse in a novice. Chronic use of tobacco is not without danger, for it is apt to produce irritation of the upper respiratory passages and of the stomach. These consist of chronic pharyngitis, laryngitis and bronchitis, and often give rise to a very disagreeable dry cough, hoarseness and attacks

of sore throat. The irritation in the mouth may produce dryness and a mild degree of inflammation of the tongue, which is said to predispose to cancer of this organ and also to epithelioma of the lips. Chronic dyspepsia, with loss of appetite and weight, is not infrequently seen in incessant smokers. Hyperacidity of the stomach may be aggravated by the constant use of tobacco.

Excessive smoking frequently causes quickening, weakness and irregularity of the heart (tobacco heart). The vision is often affected by interference with accommodation, also changes in the optic nerve and retina and temporary blindness may even occur (tobacco amblyopia). These changes in the eye usually disappear when smoking is discontinued. It is also possible that very excessive use of tobacco may be a factor in the causation of arterio-sclerosis.

SUMMARY OF GROUP ACTION.—*Stimulation of all peripheral organs depressed by atropine, including secretory glands, smooth muscle fibres and inhibitory apparatuses. Increased sweat, salivation, bronchial and gastro-intestinal secretions. Contraction of smooth muscles of intestines, bladder, ureter, gall bladder, iris and ciliary body, the effect on the two latter causes contracted pupils, spasm of accommodation and decreased intraocular tension. Increased action of the inhibitory vagus with decrease of pulse rate. Central nervous system first stimulated then paralyzed with death from failure of respiration and circulation.*

THERAPEUTIC APPLICATION.—Pilocarpine is the only member of this group which is used in practical therapeutics. The chief indications for its employment are *dropsical conditions*, especially those due to *diseases of the kidneys*. It acts by increasing the elimination of water through its stimulant action on the sweat glands. It also relieves the work of the diseased kidneys by increasing the vicarious functions of the skin.

Pilocarpine should be used only with *great caution in patients with cardiac weakness*, because of its tendency to depress the heart. It is *contraindicated in œdema of the lungs*, because by stimulating the bronchial secretion it may increase the exudation

in these organs. Its power of increasing the bronchial secretions makes it a useful *expectorant* in the first stages of *colds* or *influenza* when the mucous membranes of the bronchi are dry and congested.

Pilocarpine is used in ophthalmic practice to *contract the pupil* in cases of posterior adhesions of the iris to the lens, and to break up such adhesions. It is employed in *glaucoma* to decrease intraocular tension. For this indication it is inferior to physostigmine because the intraocular pressure is first raised before it is decreased.

On account of the stimulant action on glandular secretions, it is applied as a *hair tonic* to prevent the fall of hair, when this is due to a dry anæmic condition of the scalp.

Otologists use pilocarpine in different diseases of the labyrinth and middle ear, and it may improve dry *catarrh of the latter* by stimulating its glands.

Nicotine has been injected in the form of clysters, consisting of infusions of tobacco leaves. Occasionally the smoking of a cigar or a few cigarettes may be sufficient to move the bowels in mild constipation.

Muscarine is only of toxicological interest, but the methods of treating cases of poisoning from this alkaloid are of great importance to the practitioner. Such cases occur after the accidental ingestion of toad-stools instead of edible mushrooms. The basis of the *treatment* consists of the administration of the almost exact antidote, atropine, until the symptoms improve, in washing out the stomach, and administering a purge to remove the remaining mushrooms.

MATERIA MEDICA.

Muscarine is a strongly alkaline deliquescent alkaloid, very soluble in water, found in the fly mushrooms, Agaricus muscarius. It is related chemically to choline. Choline is also present in these mushrooms, besides a volatile substance which kills flies, and muscaridine, an alkaloid, which resembles atropine.

Pilocarpus (U.S.P.), Jaborandi Folia (B.P.) are the leaflets of Pilocarpus Jaborandi, a shrub growing in South America which contains ½ per cent. of the alkaloids pilocarpine and pilocarpidine, both of very similar chemical structure. There also occurs as a decomposition product of the former,

the alkaloid jaborine which, however, has an action similar to atropine and, therefore, does not belong to this group.

Pilocarpina is an amorphous or oily alkaloid, very soluble in water and alcohol. It forms stable salts with acids.

Pilocarpinæ Hydrochloridum (U.S.P.), white crystals, soluble in water and alcohol. It is the most commonly used preparation of pilocarpine and is often administered subcutaneously. **Dose:**—0.01–0.02 G. Average (U.S.P.) **0.01 G.**

Pilocarpinæ Nitras (U.S.P.,B.P.), properties much like the hydrochloride. **Dose:**—0.01–0.02 G. Br. ($\frac{1}{20}$–$\frac{1}{2}$ grain). Average (U.S.P.) **0.01 G.**

Nicotina is a volatile colorless liquid alkaloid found in the leaves of Nicotiana Tabacum or common tobacco.

Duboisia Hopwoodii yields the alkaloid *piturine*, while Nigella Sativa yields *nigelline*, both of these having a pharmacological action similar to nicotine.

GROUP OF PHYSOSTIGMINE.

Physostigmine (Eserine), and Eseridine, two alkaloids extracted from the calabar bean, produce symptoms resembling, to some extent, those occasioned by muscarine. They are more conveniently described in a separate group, because the seat of action is on the muscular and glandular protoplasm instead of on nerve endings, as with muscarine, and because they have a special action also upon the cardiac and striated muscles.

PHYSOSTIGMINE stimulates the protoplasm of all **muscles,** striated, unstriated and cardiac. From the stimulation of striated muscle fibres, we observe fibrillary contraction of all skeletal muscles which may even last for a considerable time after the death of an animal poisoned by physostigmine. From the stimulation of the smooth muscle fibres there occur vomiting, defecation, urination, and contraction of the ureter, spleen, bladder, uterus and pupil. From the *stimulation of the* **heart** *muscle, we see a great increase in the force and completeness of contraction* of this organ, as a consequence of which it always beats for a considerable time after respiration has stopped. The rate of the pulse is also decreased by direct action on the heart muscle, and in cases of poisoning, patients have complained of a tumultuous cardiac action. Stimulation of the protoplasm of the salivary, lachrymal and sweat **glands** produces an increase in their secretions.

The **central nervous system,** after a very brief stage of primary stimulation, is powerfully depressed, especially the centres in the medulla. The **respirations** are at first increased in depth and frequency, then, as the centre becomes paralyzed, they become superficial and dyspnœic. The blood pressure at first rises on account of a combination of circumstances as follows: firstly, the tremendous stimulation and increase in the strength of the cardiac muscles, secondly, the squeezing out of the blood from the vessels of the splanchnic area due to the cord-like contraction of the intestines, and lastly, the primary stimulation of the **vasomotor centre.** The latter, however, can be of but little importance because the depression of this centre quickly succeeds the initial stimulation. Although the blood pressure falls at last, the imminent cause of death is the paralysis of respiration.

The **cord** is also depressed and this causes the weakness and even paralysis of the limbs which is seen during poisoning by physostigmine. The **brain** is affected very late for consciousness remains almost until the end. The anxiety and restlessness usually observed is due to interference with respiration and not to stimulation of the brain and cord.

The **pupil** is contracted by direct stimulation of the iris muscle, but the contraction is not so complete as with muscarine because both sets of fibres are affected so that the weaker radial antagonize to a certain extent the action of the circular fibres. The ciliary muscle is also stimulated so that the lens is focused for near objects. By local application, contraction of the pupils appears within one hour and lasts from eight to twenty-four hours or more. The **intraocular pressure** is decreased partly in consequence of the narrowing of the pupil but chiefly by contraction of the vessels of the eyeball.

Physostigmine is **excreted** rather rapidly and mainly in the urine, although it has been found in traces in the bile and saliva.

The symptoms of **poisoning** consist of giddiness, anxiety, dyspnœa, excitement, palpitation of the heart, severe pain in the region of the stomach, nausea, vomiting and diarrhœa, salivation, perspiration, and contraction of the pupils, great weakness of the

limbs, and even inability to stand, accompanied by tremors, general muscular twitchings, and at last convulsions, unconsciousness and death from stoppage of respiration. Sometimes no vomiting occurs if the absorption is very rapid, and in such cases unconsciousness and paralysis of respiration come quickly.

The crude calabar bean, the source of physostigmine, is used by the natives of certain tribes of Africa as an ordeal, to try the criminality of accused subjects. The crucial test consists of whether or not the suspect dies after the ingestion of a certain number of the beans, but that really depends on whether or not he vomits. If the drug is expelled quickly by vomiting he may not have absorbed enough to paralyze the central nervous system, while if he retains it a long time fatal results occur.

SUMMARY OF THE GROUP ACTION.—*Stimulation of striated, cardiac and smooth muscle fibres and of the secretory glands. Resulting twitching of skeletal muscles, tremendous increase in the force of the heart beat, and spasmodic contraction of the smooth muscles of the intestines, bladder, gall bladder, ureter, spleen, etc., also increase in the secretion of the salivary, bronchial, sweat and gastro-intestinal glands. Primary stimulation of the centres in the medulla quickly followed by intense depression, producing death by failure of respiration.*

THERAPEUTIC APPLICATION.—Physostigmine has been used in the past in various diseases of the nervous system, but without much success. Unfortunately, its stimulant action upon the heart and skeletal muscles cannot be utilized because of its great depressant effect upon the medulla. Formerly it was recommended to relieve atony of the bowels. In *constipation* from this cause, physostigmine, in small doses, was said to be beneficial, but actual experiments on human beings have failed to support this use.

When applied locally to the eye, it may assist in breaking up adhesions of the iris, but its chief use is to reduce the intraocular pressure in *glaucoma*.

MATERIA MEDICA.

Physostigma (U.S.P.), Physostigmatis Semina (B.P.), or Calabar or Ordeal Bean, consists of the seeds of Physostigma Venenosa, a woody climber growing in Africa which contains 0.15 per cent. of the alkaloid physostigmine including small quantities of eseridine, an alkaloid having a close resemblance in composition and action, and also traces of the alkaloid calabarine which has an action resembling strychnine.

Physostigmina, colorless crystals, insoluble in water, slightly soluble in alcohol.

Physostigminæ Salicylas (U.S.P.), slightly yellow crystals which easily turn brown, difficultly soluble in water, but soluble in alcohol.

Physostigminæ Sulphas (U.S.P.,B.P.), white, deliquescent crystals, soluble in water and alcohol. **Dose:**—for physostigmine and its salts 0.0005–0.001. Br. ($\frac{1}{100}$–$\frac{1}{120}$ grain)not more than 0.003 in 24 hours. Average (U.S.P.), **0.001 G.** In the eye use 1 to 3 drops of ½ per cent. to 1 per cent. solution.

GROUP OF COCAINE.

The leaves of Erythroxylon Coca, a tree growing in Bolivia and Peru, have been used for a long time by the Indians of these countries to relieve hunger and to enable them to make long, fatiguing marches without exhaustion. It is probable that the increased power for muscular exertion which they experienced was due to a stimulation of the central nervous and muscular systems akin to that produced by caffeine. The diminution in the sensation of hunger resulted from a local anæsthetic action on the endings of the sensory nerves in the stomach.

Paralysis of the endings of **sensory nerves** is one of the main features in the action of **COCAINE.** It only takes place when solutions are applied locally on a mucous membrane, on abrased surface or underneath the skin. The sensation of pain and touch is more decreased than that of heat. After topical application of a 4 per cent. solution, local anæsthesia occurs in about five to ten minutes and lasts about twenty minutes.

Local applications to nerve trunks and even to the spinal cord are followed by sensory paralysis. When a solution of cocaine is painted on a nerve, all the area to which sensation is supplied is rendered anæsthetic. When it is injected in small quantities in the lumbar region of the spinal canal, sensory paralysis of the legs and trunk occurs which may permit of painless amputation

of a leg or of laparotomy. By this mode of application the paralysis is chiefly of sensation of pain, for the sense of touch, heat and cold and motor function may remain unchanged.

When sufficient cocaine has reached the circulation, the **central nervous system** is at first stimulated, but later depressed, and death takes place mainly through failure of respiration. Under these circumstances no paralysis of the peripheral sensory nerve endings occurs in warm-blooded animals, because death takes place from a much smaller quantity than would be necessary to produce this effect. At first, on account of the stimulation of the central nervous system, cocaine produces nervousness, restlessness, headache, nausea and vomiting, rise of blood pressure and temperature, hurried respirations, delirium and even clonic convulsions. Subsequently, or at times from the beginning, the following symptoms of central paralysis occur: great weakness, coldness of the extremities, dulness of the intellect, decreased respiration, fall of blood pressure, cyanosis and death.

The increase in **respiration** is due to stimulation of the respiratory centre. The latter, however, is soon depressed and death is mainly caused by its paralysis. The primary increase in blood pressure results from stimulation of the **vasomotor centre,** and from increased rate of the heart. The quickening of the pulse is probably caused by a stimulant action on the accelerator nerves. The fall of blood pressure and failure of circulation which soon ensue are due to direct paralysis of the **heart** and of the vasomotor centres.

The local application of cocaine causes a powerful contraction of the **blood vessels,** which produces in the nose a shrinking of the turbinates, in the throat and other mucous membranes a blanching and dryness of the mucosa, and in the eye a decrease in the **intraocular tension.** The **pupils** are dilated, probably by stimulation of the dilator fibres.

When cocaine is used in the eye, the cornea occasionally becomes clouded on account of necrosis of the epithelium. Because of its destructive action on protoplasm, abscesses may form after subcutaneous administration of cocaine. In mice,

necrosis and vacuolation of liver cells may take place after internal administration. These effects are probably due to general **protoplasmic poisonous action** of cocaine, because it also stops the movements of leucocytes, spermatozoa and certain vegetable cells, as does quinine.

The body **temperature** is raised, perhaps by some action on the heat-regulating mechanism.

When cocaine is taken over a period of time, a **habit** is formed as with morphine, and a craving for the drug is developed. The symptoms of chronic cocaine **poisoning** resemble closely those of chronic morphinism and consist of gastro-intestinal disturbances, anorexia, loss of weight and strength, tremors, sleeplessness, hallucinations, delirium, and sometimes convulsions.

Cocaine is almost completely **oxidized** in the body of most animals, and the small amounts which escape oxidation, are found in the urine.

In attempting to make **substitutes** for cocaine it was discovered that esters of benzoic acid especially had local anæsthetic properties. Prominent among these are **Beta-Eucain, Stovain, Novocain, Alypin, Orthoform, Anæsthesin** and **Subcutin.** All these bodies are weaker local anæsthetics than cocaine. The strongest are *stovain* and *subcutin.* Besides, may be included as substitutes of cocaine, **Tropacocain,** an alkaloid obtained from Javanese coca leaves, said to have a very similar action, also **Holocain,** a derivative of phenacetin which is very poisonous, and lastly, **Yohimbin,** an alkaloid obtained from the African Yohimbe tree. The latter is also used internally to increase sexual power in impotence in the male.

SUMMARY OF GROUP ACTION.—*By local application, paralysis of sensory nerve endings, nerve trunks and posterior spinal roots, producing sensory paralysis of the parts supplied and especially depression of the sense of pain. Primary stimulation of the central nervous system with excitement, delusions, convulsions, increased respiration and rise of blood pressure, followed by paralysis with cold extremities, weak pulse and respiration and death in coma.*

THERAPEUTIC APPLICATION.—Cocaine was formerly used in small doses on account of its primary stimulant action on the central nervous system. This use is now practically discontinued on account of the danger of forming a habit and of producing collapse in very susceptible subjects.

The main application of cocaine is as a *local anæsthetic* to quiet pain and to allow painless operations. It is used in the eye to quiet the pain from *foreign bodies*, to remove *cataracts*, to perform *iridectomy*, *enucleation*, etc. It is also employed for practically all *nasal* and *laryngeal operations* and has the advantage in the nose of shrinking up the turbinated bodies, thus allowing a better field of operation. It is used subcutaneously for minor operations and also for major operations, as laparotomy. When applied for major surgical operations it is usually given by *Schleich's infiltration method*. This consists of infiltrating a large bulk of a very dilute solution of cocaine between the layers of the skin. The local anæsthetic action is brought about partly by the specific effect of cocaine and partly by the pressure of the fluid on the sensory nerve endings.

Another method of using cocaine and some of its allies, as stovain, novocain, etc., for major operations, is by *intraspinal injections*. This consists of injecting 0.01 to 0.02 G. by lumbar puncture. Adrenaline is now usually injected with the local anæsthetics, as it increases their action and decreases their poisonous symptoms. In about half an hour the lower limbs and abdomen become completely narcotized so that amputations and laparotomies can be performed without pain. There are, however, two great objections which make this method impracticable, first, the greater shock on account of the consciousness of the patient, and second, the poisonous symptoms consisting of delirium, nausea, vomiting, headache and collapse which often follow when cocaine is applied in this way. Another very alarming symptom which occasionally occurs, is the motor paralysis of the limbs which may last from a few days or weeks to permanency. In explanation of this fact there have been found severe histological changes in the spinal cord of animals and also in those of

human beings, who died after intraspinal anæsthesia with cocaine, stovain or novocain.

MATERIA MEDICA.

Coca (U.S.P.), dried leaves of Erythroxylon Coca, a shrub growing in Bolivia, Peru and India. It contains a number of alkaloids, the chief one of which is cocaine.

Fluidextractum Cocæ. Dose:—2.0–4.0 c.c.

Cocaina (B.P.), white, crystalline alkaloid, insoluble in H_2O, soluble in alcohol. It can be broken up into ecgonine, benzoic acid and methyl-alcohol.

Cocainæ Hydrochloridum (U.S.P.,B.P.), colorless crystals, bitter and benumbing taste, soluble in H_2O and in alcohol. It is decomposed by boiling water. Used locally in ¼ to ½ per cent. solution to quiet pain, in 3 to 6 per cent. solution to allow of surgical operation or examination by instruments. The use of 10 to 20 per cent. solution is often attended by poisonous symptoms. Poisoning frequently results from local application in the urethra and bladder. It should not be used over a period of time for fear of producing habit. By Bier's intraspinal or by Schleich's infiltration methods, not more than 0.02 G. should be used. **Dose:**—0.005–0.05 G. Br. (⅙–1 grain), per day, up to 0.15 G. Average (U.S.P.) **0.03 G.**

Alpha- and Beta-Eucaine are local anæsthetics less poisonous than cocaine, but very irritant. They do not dilate the pupil, nor constrict peripheral vessels. Used in 2 to 4 per cent. solutions.

Holocaine is more poisonous than cocaine, and has no action on pupil and vessels. Used as a local anæsthetic in ½ to 1 per cent. solution.

Stovain, white crystals soluble in water and alcohol. For local anæsthetic action subcutaneously, use 0.5–1 per cent. solution, and effect comes in from one to four minutes and lasts twenty minutes; for mucous membranes of the nose and throat, use 5 per cent. solutions, and for spinal anæsthesia inject 0.05 G. into the medullary canal.

Novocainum, white crystals soluble in water; used in from ¼–2 per cent. solution.

Alypin, white crystals also soluble in water; used in 2 per cent. solution.

Orthoformium Novum, benzoic acid derivative, which is almost insoluble in water. It is not absorbed easily and does not produce poisonous symptoms, but its local anæsthetic action is very weak and superficial. Used as a 10 per cent. to 20 per cent. ointment or powder over painful ulcers, also internally in ulcers or cancers of the stomach in the form of a powder. **Dose:**—0.5–1.0 G.

Anæsthesin is another insoluble local anæsthetic with properties very closely resembling those of Orthoformium. Used both locally and internally. **Dose:**—0.3–0.5 G.

GROUP OF CURARE.

In curare, an arrow poison, which the Indians of South America prepare from various species of strychnos, there is present the alkaloid curarine and a number of closely related bodies.

All these substances have practically the same main action which consists of a *paralysis of the* **motor end plates** *of nerves supplying striated muscles* before any other organ is affected.

When **CURARINE** is injected into animals, they lose the power of muscular contraction and after attempts at walking fall, in a limp condition, to the ground. They are still able to make a number of jerky contractions of the extremities while their respirations become fewer and fewer. The power of muscular movement soon disappears completely, first from the muscles of the limbs, and lastly from those of respiration. Warm-blooded animals die when the respiratory muscles are paralyzed. After 0.00005 G. a frog may remain motionless for days, and finally recover when the poison has been excreted.

In man we have practically the same general symptoms as in animals, accompanied in the beginning by a feeling of fulness in the head with headache, by an increased secretion of sweat, tears, urine, and later by a blueness of the skin when the muscles of respiration have been paralyzed.

With small doses, in all animals, the **circulation** and **nervous system** *remain practically unaffected.* When large doses are administered, and artificial respiration is maintained, curarine paralyzes the nerve terminations around the *ganglia supplying the blood vessels, the inhibitory apparatuses of the heart* and *of the intestines.* The blood pressure falls on account of the dilatation of the vessels, incident to paralysis of their ganglia. The increased flow of blood to glands resulting from this dilatation of the blood vessels may account for the augmented secretion of urine, sweat and tears. With large doses, there is an increase in the rate of the heart beat and a greater peristalsis of the intestines, because of the paralysis of the inhibitory ganglia of these organs. In very large doses curare paralyzes the central nervous system, although in frogs it, at first, causes an increase in the reflex irritability of the cord when applied directly to this organ with the circulation destroyed. It has no effect on the **muscles** as enormous doses do not change their irritability.

Curare is **absorbed** very slowly from the stomach, so slowly

that no poisonous symptoms are seen from a dose given by the mouth, which is fatal when given subcutaneously or intravenously. The reason for this fact is that curarine is **excreted** more rapidly by the kidneys, than it is absorbed by the stomach so that a poisonous dose cannot have time to accumulate in the organism.

Sugar and lactic acid may be found in the **urine** after poisoning by curare. The presence of these abnormal products in this secretion and the destruction of glycogen in the muscles and liver, are probably due to asphyxia. The **metabolism** is greatly decreased on account of the paralysis of the muscular system, and consequently the exchange of carbon dioxide may be much lowered.

Protocurarin is also found in the crude curare. It has the same qualitative, but a much stronger quantitative action, than curarine; besides there is also present *Protocurin and Tubocurarin*, both with much weaker curare-like action than curarin. *Curin* on the other hand has almost the same effect as veratrine and does not belong to this group.

SUMMARY OF THE GROUP ACTION.—*Paralysis of motor nerve endings of all striated muscles causing death by paralysis of the diaphragm and other respiratory muscles. Large doses given while artificial respiration is maintained produce paralysis of the ganglia of blood vessels of the inhibitory apparatuses of the intestines and heart, with resulting fall of blood pressure, increased intestinal peristalsis and quickening of the rate of the heart. Absorbed very slowly by stomach but rapidly from subcutaneous tissues. Excreted rapidly by kidneys.*

THERAPEUTIC APPLICATION.—**Curare** was formerly used in conditions attended with *convulsions* such as *tetanus*, *hydrophobia* and *epilepsy*. In tetanus and hydrophobia, it must be given in doses sufficient to depress the motor nerve endings of all the skeletal muscles, yet not large enough to paralyze those of respiration. Either the pure alkaloid or the crude drug which has been standardized on frogs, may be administered in the presence of a medical attendant who should always be ready to perform artificial respiration. The reports vary, but on the whole,

the results are not satisfactory enough to warrant this form of treatment except when all others have failed.

MATERIA MEDICA.

Curare, dark brown resinous mass, soluble in water, varying much in strength. Should be standardized on frog before using. The amount necessary to paralyze a 50 gram frog is equivalent to 0.00004 G. curarine.

Curarinum Purissinum, brownish, yellow, amorphous body, soluble in water, alcohol, ether; does not form salts with acids. **Dose:**—0.0005–0.003 G. subcutaneously.

ACONITINE SERIES.

The following series is composed of the groups of Aconitine, Coniine and Veratrine which have many properties in common. They have a very striking *depressant action on the vital centres in the* **medulla** which leads to death, but this depression is usually preceded by a more or less transient stimulation of the same. Their action on the *nerve endings* of peripheral organs, as those supplying sensory, motor and secretory apparatuses is usually first, a stimulation as with muscarine, then later a depression as with atropine. With most drugs of these groups a curare-like depression of the motor nerve endings of striated muscle fibres is a prominent symptom in cold-blooded animals, but with a few members as coniine and sparteine, this action becomes well marked in the warm-blooded. The various alkaloids of this series produce dilatation of the **pupil.**

The picture of **poisoning** does not differ greatly in the different members. It consists of nausea, vomiting, diarrhœa, weakness, sweating and dryness of the skin, great dyspnœa and feebleness of the circulation with the sensorium remaining normal to the last.

As might be expected, this series of groups is of but comparatively small therapeutic value on account of the prominent depression of the vital centres, and only occasionally a few members are used for some local or special internal purposes.

GROUP OF ACONITINE.

ACONITINE produces, at first, a primary stimulation of the end apparatuses of the sensory, motor and secretory nerves which is followed by paralysis. If rubbed into the *skin* in alcoholic solution, it gives rise to a sensation of burning and prickling at the place of application which is followed by *local anæsthesia* as with cocaine. When taken internally in sufficient doses, it causes at first a burning and scratching sensation in the throat, œsophagus and stomach followed by salivation and vomiting, later by dryness and an unpleasant feeling in the mouth. Sweat may be at first profuse, but subsequently the skin becomes dry, and there is a sensation of tingling and smarting followed by a feeling of cold, diminished sensibility, great weakness, convulsions, difficult breathing, loss of sight and hearing. The respirations, at first hurried and deepened, afterwards become shallow and less frequent until they stop entirely, with almost simultaneous arrest of the circulation so that death takes place in general collapse usually preceded by unconsciousness.

The action of aconitine on the **medulla** consists of a very transient stimulation of the vasomotor and respiratory centres, followed by depression, so that a slight temporary increase in the force of the respirations and of the blood pressure is followed by a decrease.

The **heart,** at first quickened for a short time, due to stimulation of the motor ganglia, is soon slowed by stimulation of the vagus and by depression of the ganglia. Then, the pneumogastric is also depressed and the pulse becomes more rapid. Finally, with further ganglionic paralysis, the heart becomes irregular and weaker until it stops entirely.

The **temperature** is lowered by aconitine, probably due to the beginning of collapse.

Fibrillary twitchings of the skeletal **muscles** are usually present in both cold and warm-blooded animals and are due to a stimulation of the motor nerve endings. Following these symptoms, there is a complete muscular relaxation due to a curare-like

paralysis of their nerve endings, while the muscles themselves remain unaffected.

The alkaloids, **Japaconitine, Pseudoaconitine, Delphinine** and **Staphisagrine** have practically the same action as aconitine. Japaconitine and pseudoaconitine are more powerful while delphinine is very much weaker. Staphisagrine differs from the others by exerting no action on the heart.

SUMMARY OF THE GROUP ACTION.—*After a brief stimulation, powerful depression of the central nervous system with death from respiratory paralysis and fall of blood pressure. Motor ganglia and vagus of the heart, sensory, motor, and secretory nerve endings first stimulated then depressed.*

THERAPEUTIC APPLICATION.—**Aconite** preparations and aconitine were formerly much used to lower the body *temperature* and diminish the force of the heart in different *febrile conditions* attended with high pulse, but at the present time their internal use has been abandoned by the greater part of the best clinicians, because the fall of temperature which they produce is due to or accompanied by collapse, which we now regard as undesirable in any condition. They are still employed on account of their *local anæsthetic action* in the form of ointments over *neuralgic nerves*. An ointment of delphinine has been used for the same purpose and also to destroy pediculi.

MATERIA MEDICA.

Aconitum (U.S.P.), Aconiti Radix (B.P.), tubers of Aconitum Napellus which resemble horse-radish in appearance and taste. They contain the alkaloid aconitine, not less than 0.5%.

Aconitina (U.S.P.,B.P.) is a white crystalline or amorphous body soluble in alcohol, insoluble in H_2O, easily decomposed into benzaconine and acetic acid. The pure alkaloid has proved fatal in the dose of 0.004 G. **Dose:**—Average (U.S.P.), **0.00015 G.**

Tinctura Aconiti (U.S.P.,B.P.). **Dose:**—0.2 c.c. Br. (5–15 ♏). Average (U.S.P.), **0.2 c.c.**

Unguentum Aconiti (B.P.).

The alkaloid **Japaconitine** is found in Japaconitum, a Japanese aconite. **Pseudoaconitine** is found in Aconitum Ferox, while **Delphinine** and **Staphisagrine** are found in Delphinium Staphisagria.

GROUP OF CONIINE AND SPARTEINE.

Besides Coniine, we place in this group the alkaloids Gelsemine, Lobeline and Sparteine on account of a great similarity of action.

CONIINE, like aconitine, depresses powerfully the **central nervous system,** after a brief primary stimulation. By its action the *respirations* are at first deepened and quickened, due to stimulation of the centre, but this stimulation is soon replaced by depression, causing death by asphyxia.

The symptoms of **poisoning** are not unlike those of aconite and consist of a tingling sensation followed by anæsthesia, a feeling of cold and great weakness, usually accompanied by vomiting and diarrhœa. Fibrillary twitchings of the muscles, tremors and even convulsions may also occur. The cerebrum is not affected early, as consciousness may persist almost until death.

This alkaloid produces first a stimulation, then a depression of the end apparatuses of the secretory, sensory and motor **nerve endings.** The seat of action is probably, as with nicotine, the ganglionic endings. As a consequence of this stimulation, we may observe salivation, nausea, vomiting and defecation.

Coniine paralyzes the motor nerve endings of **striated muscles** in cold-blooded animals, just as curare. This action is but imperfectly seen in the warm-blooded, because death takes place too rapidly from paralysis of the respiratory centre.

The **heart** is first slowed by stimulation of the vagus, but later, it is quickened by depression of this nerve. The **pupils** are dilated, probably by local paralysis.

The alkaloid **GELSEMINE** has an action almost identical with coniine, but is a much more powerful poison.

LOBELINE acts in many respects like nicotine. When administered to warm-blooded animals, it causes an increase in the rate and depth of the respiratory movements, augmented reflex irritability, salivation and vomiting, and at last a cessation of respirations. Lobeline differs from coniine, as it stimulates to an appreciable degree the medulla, especially the **respiratory**

centre, and also, to a certain extent, the spinal cord. The stimulation of the medulla causes the increase in respiration and vomiting, while the increase in reflex irritability is due to stimulation of the cord. Ultimately, however, the central nervous system, particularly the respiratory centre, is paralyzed as with coniine. A peculiarity of lobeline is that it paralyzes the endings of the **vagus in the lungs** and therefore, has a tendency to diminish or check spasm of the smaller bronchi. Its action upon the **heart** or **pupils** is the same as that of coniine.

SPARTEINE produces almost the same effect on the central nervous system as coniine, but is much weaker than the latter. It diminishes the force of contraction of the **heart** and paralyzes the **vagus.** In dogs, the pulse is at first accelerated, because of the paralysis of this nerve, while in rabbits and cats the depression of the motor ganglia is paramount and the pulse is slowed as well as weakened from the beginning.

The depression of the **motor nerve endings** of striated muscles is an important feature in the action of sparteine and the paralysis of the diaphragm due to this curare-like action, is probably the cause of death after small poisonous doses, while after larger ones, death takes place from paralysis of the respiratory centre.

SUMMARY OF GROUP ACTION.—*Just as in the preceding group, primary stimulation of the central nervous system followed by great depression and collapse. The vagus as a rule, first stimulated then depressed. Sensory, motor and secretory nerve endings stimulated then depressed. Motor nerve endings of striated muscles so much depressed that with some members this becomes a factor in the production of death. Pupils dilated.*

THERAPEUTIC APPLICATION.—**Coniine** or poisonous hemlock, has no therapeutic application and is only of interest historically as being the poison used by the ancient Greeks to carry out the death sentence, and also because it has given rise to frequent cases of poisoning in modern times by being eaten accidentally in place of chervil or parsley, both of which it resembles in botanical appearance.

Gelsemium preparations were formerly used to *dilate the*

pupil, but they have been entirely substituted by atropine, as they caused marked local irritation.

Lobelia is employed in the treatment of *asthma* on account of its action on the ends of the vagus in the lungs and on the respiratory centre. It is supposed to produce good effects in this disease by dilating the constricted bronchi and by increasing the depth of respirations, thus allowing more air to enter the lungs.

Sparteine was formerly administered to increase the force of the heart, which it does not do. It was also used as a diuretic. It has no such action, but the crude drug, the broom-plant, from which it is obtained contains a diuretic substance, **Scoparin.**

MATERIA MEDICA.

Conium (U.S.P.), Conii Fructus (B.P.), green fruits of Conium Maculatum or poisonous hemlock, grows in Europe, Asia and Africa, and contains the liquid, oily alkaloid coniine and also methylconiine. This was the poison used by the Greeks to execute Socrates.

Gelsemium (U.S.P.), Gelsemii Radix (B.P.), roots of Gelsemium Sempervirens or Yellow Jasmine. Contains the alkaloid gelsemine and gelseminine. Only the latter, the amorphous gelseminine, possesses the action of this group.

Fluidextractum Gelsemii (U.S.P.). **Dose:**—Average (U.S.P.), **0.05 c.c.**

Tinctura Gelsemii (U.S.P.,B.P.). **Dose:**—1.0–2.0 c.c. Br. (5–15 ♏). Average (U.S.P.), **1.0 c.c.**

Scoparius (U.S.P.), Scoparii Cacumina (B.P.), the tops of the broom-plant Spartium Scoparius growing in Asia and Southern Europe. It contains the colorless liquid alkaloid sparteine and also the yellow amorphous scoparine which is said to have diuretic action.

Succus Scoparii (B.P.). **Dose:**—1–2 fl.ʒ.

Sparteinæ Sulphas (U.S.P.), white crystalline body with a bitter saline taste, soluble in water and alcohol. **Dose:**—Average (U.S.P.), **0.01 G.**

Lobelia (U.S.P.,B.P.), leaves and tops of Lobelia inflata or Indian Tobacco. Contains the alkaloid lobeline.

Tinctura Lobeliæ (U.S.P.). **Dose:**—Average (U.S.P.), expectorant, **1.0 c.c.**, emetic, **4 c.c.**

Tinctura Lobeliæ Ætherea (B.P.). **Dose:**—5–15 ♏.

GROUP OF VERATRINE.

The most typical part of the action of **VERATRINE** on frogs is seen upon the muscular system. This action consists of a great *slowing of the relaxation period of the* **muscles** without any

change in their rapidity of contraction. This condition is counteracted by both fatigue and cold; for either of these will make the veratrinized muscle relax normally. It is much more difficult to induce fatigue in a veratrinized muscle than in a normal one.

Under the influence of veratrine a frog may jump naturally, but afterwards it draws up its legs to the trunk with great difficulty on account of the decrease in the power of relaxation of the extensor muscles.

Veratrine first stimulates the *peripheral endings of sensory, glandular and motor nerves*, and also the **central nervous system.** This stimulation is soon replaced by a depression of all these parts.

When a poisonous dose has been ingested by a human being, he first feels a burning and prickling sensation in the throat and stomach, which is followed by the same feeling over the entire body, by vomiting and by defecation, which may be bloody. These symptoms, as well as the sneezing which results from the inhalation of the powdered drug, are caused by the stimulation of the nerve endings. A sensation of numbness due to depression of the sensory nerves follows these symptoms of primary stimulation.

The pulse at first is slow and full, due to the peculiar action of veratrine upon the **heart muscle,** and to the rise of blood pressure incident to the stimulant effect on the vasomotor centre. After this primary stimulation, the **vasomotor** and **respiratory centres** become depressed and the subject becomes pale, his pulse feeble and irregular. He feels great weakness which is due to the depression of the central nervous system. He may be seized with convulsions and fibrillary twitchings. His respirations become fewer and shallower. His heart grows gradually weaker on account of the depression of the cardiac motor ganglia. Consciousness remains almost intact until death, which takes place in this general collapse. The action on the circulation of warm-blooded animals is complicated by a stimulation of the **vagus** followed by a paralysis, just as with aconitine.

The stimulation of the **secretory glands** is well seen in frogs by a coating of foam over the skin, and in dogs and cats by marked increased salivation. Dogs exhibit very strikingly an embarrassed spastic gait, due to the peculiar action of veratrine on muscles.

PROTOVERATRINE differs only from veratrine in that it does not paralyze the terminations of the motor nerves and does not prolong the relaxation period of skeletal or cardiac muscles. It is also much more poisonous.

SUMMARY OF GROUP ACTION.—*Central nervous system powerfully depressed after a primary stimulation just as by aconitine. Also same action on endings of sensory, motor and secretory nerve endings. Special action on striated muscles decreasing their relaxation period. Heart also slowedby a "veratrine action" on the cardiac muscles.*

THERAPEUTIC APPLICATION.—**Veratrine,** like aconitine, is used mainly externally in the form of an ointment, as a *local anæsthetic* over *neuralgic nerves*. The crude preparations of **veratrum viride** and **veratrum album** were formerly employed for the same purposes as those of aconite, i. e., to *reduce fever* and lower the rate of heart beat, but the same objections apply to such a use as to that of aconite.

MATERIA MEDICA.

Veratrina (U.S.P.,B.P.), a mixture of alkaloids prepared from Sabadilla seeds or Asagræa Officinalis (U.S.P.) or Schœnocaulon Officinale (B.P.), including crystalline veratrine or cevadine, amorphous veratrine or veratridine and sabadilline or cevadilline. The mixture forms a whitish-gray, semicrystalline powder with an acrid taste producing a tingling, benumbing sensation in the tongue.

Unguentum Veratrinæ (U.S.P.,B.P.).

Oleatum Veratrinæ (U.S.P.).

Veratrum Viride (U.S.P.), American Hellebore, contains besides veratrine, jervine, pseudojervine, etc.

Tinctura Veratri (U.S.P.). **Dose:**—0.5–2.0 c.c. Average (U.S.P.) 1.0 c.c.

Veratrum Album, white Hellebore, contains protoveratrine, jervine, pseudojervine, etc. It is used on the continent in place of veratrum viride.

GROUP OF COLCHICINE.

COLCHICINE produces severe irritation of the **gastro-intestinal tract** in a few hours after the ingestion of a sufficient dose. This results in great abdominal pain, cramps, vomiting and diarrhœa. At first, only the normal contents of the stomach and bowels are expelled, but later the excreta are composed of mucus and blood. Severe colics and tenesmus arise and the subject falls into a state of collapse, accompanied by a difficulty in moving at first the lower, and later the upper limbs. After death the mucosa of the alimentary canal is found to be greatly inflamed and it even shows ecchymoses.

In animals, bloody urine with albumen and casts or even total suppression may be observed from the severe inflammation of the **kidneys.** This irritation may explain why a few centuries ago colchicum was used in small doses to stimulate the action of these organs and relieve dropsical conditions.

The effect on the gastro-intestinal tract and kidneys takes place equally well after subcutaneous administration, although it may be delayed for a few days, only showing at first inflammatory reactions at the place of injection. Aside from evidences of inflammation there is no change in the secretion of urine, especially no constant alteration in the quantity of **uric acid,** so that the action on the latter and gout is not supported by scientific observations.

The **central nervous system** is depressed, and with sufficient doses death occurs from paralysis of *respiration*, although the cerebrum is but little affected as consciousness persists until the end. A diminution of *cutaneous sensation* is observed in the early stages of poisoning in dogs, although local anæsthesia does not result from topical application.

In an ordinary case of poisoning in mammals, the **heart** is not profoundly affected, but in frogs, colchicine produces the same action as veratrine upon this organ, i. e., a shortening of the relaxation period. The **skeletal muscles** also show the typical veratrine action.

Colchicine is changed in the bodies of warm-blooded animals to *dioxycolchicine*. Such a change does not take place in the cold-blooded. Since colchicine acts but slowly in warm-blooded animals, and almost not at all in the cold-blooded, unless it has been previously oxidized, it is believed that the action of colchicine is due to its oxidation product.

COLCHICEINE also present in colchicum has the same action as colchicine, but in a milder degree.

SUMMARY OF GROUP ACTION.—*Intense irritation of the gastro-intestinal tract and kidneys. At first, very little effect upon the central nervous system and heart, but later, death from paralysis of respiration. In animals, decrease in cutaneous sensation not due to paralysis of peripheral nerve endings. In frogs, veratrine action on heart and skeletal muscles.*

THERAPEUTIC APPLICATION.—The first use of **colchicum** in therapeutics was as a *diuretic* in dropsical conditions; then this application was laid aside and it was given chiefly in *gouty* and *rheumatic affections*, but of late it has not been so popular because of its frequent failure to cure and also because if often occasions very troublesome inflammations of the gastro-intestinal tract. It is possible that colchicum improves some cases of gout by its analgesic power, or it may be that the good effects sometimes observed come from some influence on the general metabolism.

MATERIA MEDICA.

Colchici Cormus (U.S.P.) and **Colchici Semen** (U.S.P.,B.P.), the root and seeds of Colchicum Autumnale or meadow saffron, a plant growing in Europe and North Africa. It contains two active bodies, colchicin and colchiceine.

Vinum Colchici (U.S.P.,B.P.). **Dose:**—0.5–2.0. Br. (10–30 ♏). Average (U.S.P.), **2.0 c.c.**

Colchicina (U.S.P.) is an amorphous, white or yellow nitrogenous body with an acid reaction, which crystallizes out of chloroform with two molecules of the latter. It is the methyl ester of colchiceine and is soluble in alcohol and water. **Dose:**—Average (U.S.P.), **0.0005 G.**

GROUP OF EMETINE AND APOMORPHINE.

We include in this group different substances which are used in practical medicine, in large doses, to induce vomiting or in

small doses, to increase the bronchial secretion. This increase is a secondary action brought about by the first stage of nausea and is equivalent to that observed in spontaneous nausea and vomiting or in seasickness.

The chief members of the group are certain alkaloids, Emetine and Cephaline found in Ipecacuanha, Quebrachine, Aspidosamine, etc., found in the Quebracho bark, and lastly Apomorphine, the artificial emetic, made by boiling morphine with hydrochloric acid.

EMETINE when given to a man in small doses, produces a feeling of *nausea* and a marked *increase in the bronchial secretions*, but if the dose is large, **vomiting** occurs in from half an hour to an hour and may be repeated a few times until the drug has been all ejected from the stomach. Diarrhœa frequently accompanies vomiting, and in dogs, marked inflammation of the stomach and intestines is usually observed. On postmortem examination, the mucous membrane is swollen, reddened and contains many ecchymoses just as after arsenical poisoning. Such evidences of irritation of the **gastro-intestinal tract** may even be observed after subcutaneous administration, a fact which tends to show that this drug is excreted, at least in part, by the stomach and bowels. The site of injection also shows marked inflammation and often pustulation. The **kidneys** are frequently irritated.

All these evidences of **local irritation** and the fact that the vomiting is not very prompt, suggest that the emesis is due to a local action on the stomach rather than to stimulation of the vomiting centre.

In warm-blooded animals the blood pressure is lowered, and death takes place from paralysis of the **heart** when emetine is given in sufficient doses intravenously or subcutaneously. Cold-blooded animals also show a paralysis of the heart muscle, of the central nervous system and a decrease of the irritability of the striated muscles.

APOMORPHINE is the most excellent emetic, for it acts in a specific way by *stimulation of the* **vomiting centre.** When given to a man or dog subcutaneously in sufficient doses, it causes pro-

fuse vomiting within three to ten minutes, usually accompanied and preceded by the symptoms of emesis, i. e., nausea, great weakness, muscular relaxation and accelerated pulse. These may at times be entirely omitted. Occasionally the weakness is so great that actual collapse occurs.

The action is not so rapid by internal administration, because it takes longer for absorption and reaches more slowly the centre of vomiting. Very small doses, taken internally, may produce only nausea, muscular relaxation, *increase in the bronchial and salivary secretions* and in the pulse rate.

Large doses administered to warm-blooded animals cause marked stimulation of the central nervous system, especially of the **brain** and **medulla.** Rabbits and cats become restless and their breathing is hurried. They move about to and fro violently and even go into convulsions. These symptoms of excitement at last pass away and the animals fall on the side relaxed, and *die from paralysis of respiration.*

Paralysis of the **striated muscles** and **heart** is a striking symptom in frogs, but not in warm-blooded animals.

Apomorphine is **excreted** neither by the stomach nor bronchial tract, and in fact it is not found in any of the excretions. It is probable that the increase in bronchial secretions is due to the first stage of nausea, rather than to direct action.

The **Quebracho Alkaloids,** Aspidospermine, Aspidospermatine, Aspidosamine, Quebrachine, etc., produce practically the same symptoms as apomorphine. Among these only Aspidosamine produces vomiting after subcutaneous administration. This action is, as that of apomorphine, also on the vomiting centre. All these alkaloids produce marked local irritation.

SUBGROUP OF SAPOTOXIN AND SOLANINE.

SAPOTOXINS are active glucosides found in plants as Saponaria, Sarsaparilla, Quillaja, Senega and Cyclamen, which although soluble in water are not absorbed from the gastro-intestinal tract.

When taken internally in large doses they produce severe

irritation of the **gastro-intestinal tract,** resulting in nausea, increase in bronchial secretions, vomiting, pain in the abdomen and diarrhœa.

When injected subcutaneously or intravenously, besides irritating the place of application, they produce in small doses symptoms of gastro-intestinal and renal inflammation, and in larger doses convulsions due to stimulation of the **central nervous system.** Finally, they cause failure of respiration and the other symptoms resulting from paralysis of the central nervous system.

Applied directly to the **blood,** even in very great dilution, they dissolve the red corpuscles. They paralyze striated and cardiac frog **muscles** just as do emetine, apomorphine and the quebracho alkaloids.

SOLANINE, the poison found in germinating potatoes and in other members of the Solanaceæ family, resembles the sapotoxins in its action.

It is a very powerful **local irritant** which may produce abscesses at the site of injection, also violent vomiting and diarrhœa if given internally. It is absorbed with great difficulty, so must be given intravenously in order to observe the general action.

This consists, at first, of a stimulation of the **central nervous system** followed by paralysis. After a stage of convulsive muscular contraction and general convulsions, there come deep coma and *death due to respiratory failure.*

After intravenous injection, solanine causes a breaking up of the red blood corpuscles with hæmoglobinuria and acute parenchymatous nephritis.

In different cases of **poisoning** in man from taking solanine internally to study its effects, or after eating germinating, unripe or decaying potatoes, the symptoms have been nausea, vomiting, diarrhœa with great colic and abdominal tenderness, sleepiness, dizziness, sometimes cramps in the extremities, and difficulty in breathing.

HELVELLIC ACID found in the edible mushrooms, the morels, at times gives rise to cases of poisoning, when the latter are eaten improperly prepared. Being very soluble in water, helvellic

acid is easily dissolved out of the mushrooms by boiling with water; this makes them entirely harmless. Drying and keeping for a period of time, also destroys the poisonous principle.

The symptoms of **poisoning** in man consist of violent vomiting, sometimes accompanied by diarrhœa, dulling of the intellect, stupor, delirium, dilated pupils, convulsions, and at times a slight icteric coloration of the skin. Beyond the mild icterus no other evidence of destruction of red corpuscles occurs.

The prominent symptom in dogs after intravenous injection is a destruction of **red blood corpuscles** which gives rise to a deposition of the hæmoglobin in all the organs. The **kidneys** are much irritated and their secretion contains albumen, blood, coloring matter and casts.

SEPSIN, a basic body obtained from decomposed meat, yeast and so forth, and produced by the Proteus Vulgaris, has a pharmacological action very closely resembling that of emetine.

When administered internally to a dog, it causes nausea and vomiting and is quickly expelled. If, however, it is given subcutaneously or intravenously, it causes also irritation of the **gastro-intestinal tract** which takes the form of vomiting and diarrhœa, consisting at first of the normal contents, then of a bloody fluid and even at last of pure blood. It causes death, either from the collapse incident to the violent gastro-intestinal disturbances, or in large doses from direct paralysis of the **central nervous system.**

At autopsy, it is found that the seat of action is chiefly at the pyloric end of the stomach, at the duodenum and rectum, while the Peyer's patches which are so much affected by ricin escape intense inflammation. Besides those ecchymoses present in the intestines, there are also some in the lungs, liver and spleen; the latter may contain hemorrhagic infarcts.

It is probably a fact that many of the milder cases of poisoning from tainted meat, which show only gastro-intestinal symptoms, are due to the presence of sepsin; but this form of poisoning must not be confounded with botulism which is much more serious and exhibits many nervous symptoms.

SUMMARY OF ACTION OF EMETINE GROUP AND SAPOTOXIN SUBGROUP.—*The production of emesis with its attending symptoms, increased bronchial secretion, nausea, muscular relaxation, general weakness and quick pulse. Irritation of the intestinal tract leading to diarrhœa. Depression of the heart and striated muscles and also of the central nervous system after subcutaneous administration.*

THERAPEUTIC APPLICATION.—Formerly vomiting was in current use for almost all sicknesses. Then, flourished ipecac; but nowadays, we find so few indications for it that the members of this group have lost much of their importance in therapeutics. Even in cases of poisoning, one of the few occasions to cause emesis, we usually prefer the stomach tube.

In the nauseated stage preceding vomiting, the bronchial secretion is always increased so that all emetics can be used in very small doses as expectorants.

Among the members of these groups, crude preparations of **quillaja, senega, sarsaparilla** containing sapotoxines and saponines, also **quebracho** and **ipecac** are especially applicable for *expectorant* use, but on account of the disagreeable, nauseated, weak feeling which they cause, are inferior to the direct expectorant, as for example, the ammonium salts.

Apomorphine, which is crystalline and rapidly absorbed, is not so suitable as an expectorant, because its action is too rapid and of too short duration. It is the ideal *emetic*. It produces vomiting in man in from five to ten minutes after a dose of 0.005 G. It is sometimes used in cases where there is an indication to empty the stomach of offending material, as of poisoning by drugs or decomposed food. Its use is contraindicated in narcotic poisoning because the vomiting centre may be paralyzed and incapable of stimulation.

Ipecac preparations are used mainly as *emetics* for children and in small doses as *expectorants* for adults. They are sometimes employed in minute quantities to stimulate the gastric mucous membranes in atony of the stomach. Ipecac has been recommended as a valuable remedy for *tropical dysentery*. It

may act in such cases purely as a local irritant in stimulating the processes of repair, or it may influence the causative agent. It is used especially in the form of Dover's powders to produce sweating in *acute colds*. The sweating is probably of a reflex origin from irritation of the gastro-intestinal tract.

Besides its use as an *expectorant*, **sarsaparilla** has been employed a great deal in the disease *syphilis*. It was at one time thought to have specific action, but now we believe that what benefit may be produced can be attributed to the improvement of the general metabolism on account of the stimulant action on the gastro-intestinal tract. It also serves as a vehicle for the administration of badly tasting drugs.

MATERIA MEDICA.

Ipecacuanha (U.S.P.), roots of Cephaëlis Ipecacuanha, a small shrub growing in Brazil, Bolivia and Peru, and Ipecacuanhæ Radix (B.P.), the dried roots of Psychotria Ipecacuanhæ. They contain the alkaloids emetine and cephaëline, both of which are quinoline derivatives. Emetine is easily decomposed, by standing, into a brown body, which has lost its powers, and is therefore not used in medicine. **Dose:**—As emetic. Average (U.S.P.), **1.0 G.** Br. (15–30 grains). As expectorant. Average (U.S.P.), **0.065 G.** Br. (½–2 grains).

Syrupus Ipecacuanhæ (U.S.P.). **Dose:**—Average (U.S.P.), **1.0–16.0 c.c.**

Vinum Ipecacuanhæ (U.S.P.,B.P.). **Dose:**—Average (U.S.P.), **1.0 c.c.** Br. (10 ♏—6 fl.ʒ).

Aspidosperma or Quebracho is the bark Aspidosperma Quebracho, a tree growing in Argentine and Chili. It contains the following alkaloids, aspidosamine, aspidospermine, aspidospermatine, quebrachine, hydroquebrachine and quebrachamine.

Fluidextractum Aspidospermatis. **Dose:**—0.3 c.c.

Apomorphinæ Hydrochloridum (U.S.P.,B.P.), is composed of minute, grayish crystals, soluble in 39 parts of water, turns dark by exposure to light without loss of strength. It is made by heating morphine with hydrochloric acid and is chemically morphine less one molecule of water. **Dose:**—0.005–0.015 G. Br. ($\frac{1}{20}$–$\frac{1}{10}$ grain). Average (U.S.P.) expectorant, **0.002 G.**, emetic, **0.005 G.**

SAPONIN BODIES.

Sarsaparilla (U.S.P.), is the root of Smilax Officinalis and Sarsæ Radix (B.P.), large climbers growing in tropical America. They contain the active glucoside parillin and also saponin.

Fluidextractum Sarsaparillæ (U.S.P.). **Dose:**—2.0–5.0 c.c. Average (U.S.P.), **2.0 c.c.**

Extractum Sarsæ Liquidum (B.P.). **Dose:**—2–4 fl.ʒ.

Syrupus Sarsaparillæ Compositus (U.S.P.). **Dose:**—10.0–15.0 c.c. Average (U.S.P.), **16.0 c.c.**

Quillaja (U.S.P.), Quillajæ Cortex (B.P.), is the inner bark of Quillaja Saponaria, a tree growing in South America and India. It contains besides the inoffensive saponin, the very poisonous quillaja sapotoxine and quillaic acid.

Fluidextractum Quillajæ (U.S.P.). **Dose:**—Average (U.S.P.), **0.2 c.c.**

Tinctura Quillajæ (B.P.). **Dose:**—2.0–5.0 c.c. Br. (30–60 ♏).

Senega (U.S.P.), Senega Radix (B.P.), is the root of Polygala Senega, a tree growing in the United States and Canada. It contains senegin, polygalin and saponin.

Fluidextractum Senegæ (U.S.P.). **Dose:**—0.5–2.0 c.c. Average (U.S.P.), **1.0 c.c.**

Syrupus Senegæ (U.S.P.). **Dose:**—5.0–8.0 c.c. Average (U.S.P.), **2.0 c.c.**

Tinctura Senegæ (B.P.). **Dose:**—½–1 fl.ʒ.

GROUP OF ERGOTOXINE.

For many years, extracts of **ergot,** the parasitic fungus which grows on rye or maize, have been employed to aid labor in pregnant women, also to arrest hemorrhage after parturition.

The ingestion of ergotized rye and maize which is prevalent in certain parts of southern Russia and Italy, has given rise to quite severe epidemics of poisoning. These take the form of two types: the gangrenous, accompanied by dry necrosis of tissues, and the convulsive, accompanied by spasmodic seizures and contractions.

Until the masterly work of Barger and Dale, scores of active principles were attributed to ergot and among these figures sphacelotoxin, cornutin, secalin, ergotin, etc. At present we know definitely from the research of these experimenters that the characteristic action of ergot is due to the alkaloid, **ergotoxin,** and to a smaller extent to **tyramine,** a body resembling closely adrenalin in both chemical structure and action.

Ergot and the active principle, ergotoxin, induce marked contraction of the **uterus,** due to stimulation of the motor-nerve endings. This effect is more marked in pregnant animals and may induce abortion. Given during labor, ergot may materially aid the expulsion of the fetus and after labor it may prevent postpartum hemorrhage by contracting the relaxed uterus and closing

the bleeding sinuses. Tyramine, like adrenalin, sometimes contracts the uterus and sometimes relaxes it, because it has in addition to the action on the motor-endings, a marked one on the inhibitory nerves.

Both alkaloids produce an action absolutely analogous to that of adrenalin upon the **circulation.** They cause a great immediate rise of blood pressure due to constriction of all peripheral blood vessels, which in turn is the result of stimulation of the constrictor nerve-endings in the vessel walls. Prolonged administration of these substances may produce such powerful and long-lasting constriction of the smaller vessels, that hyaline thrombosis and gangrene may result. In animals, classical experiments upon cocks' combs and pigs' ears invariably demonstrate this action. Very few doses given internally are necessary to produce gangrene of the rooster's comb.

The **pupils** undergo a powerful constriction after the intravenous application of these substances, although the same may be preceded by a momentary dilatation. This constriction is due to direct effect on the muscle fibers.

Some evidence of medullary stimulation is seen in the slowing of the heart. It has not been proved whether the convulsions are due to stimulation of the convulsive centers or of the cord. Large single doses seem to produce death from paralysis of the central nervous system.

The vomiting and diarrhea which is sometimes observed after ergot may be the result of the action of the sapotoxins present in crude preparations or of the specific alkaloids themselves.

ERGOTINIC ACID, another constituent of ergot, has none of the action of this group. It acts like the sapotoxines and merely produces irritation of the gastro-intestinal tract, but no general symptoms after internal administration. Yet, after subcutaneous or intravenous injections, it produces paralysis of the nervous system just as the sapotoxins.

Acute ergot poisoning in man, consists mainly of gastro-intestinal irritation with nausea, vomiting and diarrhœa, and of

stupor, collapse and death from failure of respiration; the latter may be preceded by convulsions.

Chronic poisoning, which occurs in countries where ergoted rye or maize is eaten, can be divided into two types, the convulsive and the gangrenous.

The **convulsive** type begins with headaches, heaviness of the head, dizziness, roaring in the ears, and the especially characteristic symptom of formication which lasts through the whole disease; also, a feeling of anæsthesia in the fingers and toes, great thirst, vomiting, colics, diarrhœa and in the severer cases twitchings and painful clonic and tonic contractions of different muscles, especially the flexors. Tetanic or epileptiform attacks occur until death results, either from exhaustion or from the convulsions.

The **gangrenous** type presents about the same symptoms at the beginning, but in a few days or weeks, there occurs in different parts of the limbs a feeling of cold and deadness followed by dry gangrene. The toes and feet are more likely to be affected than the fingers and hands. Whole toes may drop off and death may result from exhaustion or secondary infection.

SUBGROUP OF HYDRASTINE.

HYDRASTINE, from Hydrastis, produces at first, a stimulation of the **medulla** and then of the **cord** which result in increased respiration, a rise of blood pressure, a slowing of the pulse and convulsions. These symptoms are quickly followed by those of paralysis and there occurs decreased respiration, increase in pulse rate and fall of blood pressure. The latter is due to both depression of the medulla and paralysis of the **heart muscle.** The rise of arterial tension may be elicited with doses insufficient to cause increase in reflexes or general paralysis.

HYDRASTININE, an artificial substance, formed from hydrastine, produces much less action on the **central nervous** system than the latter, although in large doses it also produces death from **paralysis of respiration.**

It always causes a contraction of **peripheral blood vessels,**

due both to local and central action, in a more marked degree than hydrastine.

It does not paralyze the **heart** as does its antecedent, but may even augment its strength. It also increases the power of the skeletal **muscles** in frogs, but it has not been shown to improve the contractions of the **uterus.**

SUMMARY OF ACTION OF THE ERGOTOXINE GROUP AND HYDRASTINE SUBGROUP.—*Powerful contraction of the pregnant uterus and also of smooth muscles in the walls of blood vessels; the former aiding expulsion of the contents of uterus and diminishing hemorrhage of this organ; the latter increasing the general blood pressure. At first, stimulation of the central nervous system followed by depression with death from failure of respiration. Chronic ergot poisoning consisting of two types, convulsive and gangrenous.*

THERAPEUTIC APPLICATION.—On account of the contracting action on blood vessels, the substances of these groups, especially in the form of crude preparations of **ergot** and **hydrastis,** have been used a great deal in former times to arrest *hemorrhage* from internal organs. This use is not strictly rational because the contraction of vessels is accompanied by a rise of blood pressure which would obviously tend to overcome the good effects, i. e., decrease in amount of bleeding and formation of clot: therefore favorable results were rarely obtained.

Nowadays, these drugs are used almost exclusively for *hemorrhage in the uterus.* Here the action is very marked because besides a contraction of the vessel wall, we have at least in the case of ergot, a contraction of the uterine fibres around the bleeding vessels which closes their apertures.

Ergot is employed to arrest hemorrhage in the uterus from any cause, but especially after *parturition.* It is also used to remove *submucous fibroids* and this result is brought about by cutting off their blood supply. It is of service to aid the *subinvolution of the uterus* after child birth or abortion.

Hydrastis and its preparations are used mainly to arrest hemorrhage from the uterus not connected with pregnancy, and

to decrease too *profuse menstruation*. Crude preparations of hydrastis are also used as tonics on account of the bitter berberine which they contain.

MATERIA MEDICA.

Ergota (U.S.P.,B.P.), sclerotium of Claviceps Purpurea, is a fungus replacing grains of rye. It grows in Southern Europe and contains Ergotoxine, Tyramine and Ergotinic Acid.

Fluidextractum Ergotæ (U.S.P.). **Dose:**—2.0–4.0 c.c. Average (U.S.P.) **2.0 c.c.**

Extractum Ergotæ (U.S.P.,B.P.). **Dose:**—0.3–1.0 G. Br. (2–8 grains.) Average (U.S.P.) **0.25 G.**

Vinum Ergotæ (U.S.P.). **Dose:**—4.0–16.0 c.c. Average (U.S.P.) **8.0 c.c.**

Hydrastis (U.S.P.), Hydrastis Rhizoma (B.P.), or Golden Seal, roots of Hydrastis Canadensis which contains the alkaloids hydrastine, berberine and canadine. Canadine is present in such small traces that it does not influence the action of the crude drug. It acts like morphine. Berberine is almost inactive.

Hydrastina is a white crystalline alkaloid, soluble in alcohol and insoluble in water.

Hydrastininæ Hydrochloridum (U.S.P.), artificial alkaloid formed by the oxidation of hydrastine. **Dose:**—0.01–0.05 G. Average (U.S.P.) **0.03 G.**

Fluidextractum Hydrastis (U.S.P.). **Dose:**—0.3–4.0 c.c. Average dose (U.S.P.) **2.0 c.c.**

Tinctura Hydrastis (U.S.P.,B.P.). **Dose:**—0.5–2.0 c.c. Br. (15–60 ♏). Average (U.S.P.) **1.0 c.c.**

Glyceritum Hydrastis (U.S.P.). **Dose:**—0.3–4.0 c.c. Average dose (U.S.P.) **2.0 c.c.**

Stypticin (Methoxyhydrastinine), is the same as *cotarnin* and is obtained by decomposing narcotin. It is a white crystalline body with physiological action and uses similar to hydrastinine. **Dose:**—0.02–0.03 G.

GROUP OF DIGITOXIN.

"Heart poisons" or "heart tonics" are the names sometimes given to the large list of substances belonging to this group. The best known and most characteristic members are the active principles extracted from the leaves of Digitalis or Foxglove, i. e., Digitoxin, Digitalin and Digitalein.

Crude drugs containing various members of this group were employed by the Ancients; but the action on the pulse was first described by the English clinician Withering in the 18th century. Although he recommended digitalis only as a diuretic

to remove accumulated fluid, yet he claimed that the good effect was best seen when the pulse was weak and that its use was followed by a great increase in the quantity of urine voided, accompanied by a marked strengthening in the force of the pulse with a diminution in its rate.

When a solution of **DIGITOXIN** is administered to a fenestrated frog, there is to be observed, at first, a great increase in the force of contraction of the **heart.** It becomes white in systole on account of the very complete emptying of the ventricles; the rate of beat is much slowed; later, it becomes irregular and peristaltic waves are seen going over the organ, and, at last, the heart stops suddenly and completely contracted in systole. If at this moment the organ is distended by a column of fluid, it starts to beat again very energetically as long as the pressure is increased to a certain point, and when this point is reached, the heart loses its irritability and stops for good. These facts seem to show that the stoppage of the frog's heart in systole is not due to a loss of contractility but rather to a loss of elasticity. This loss of elasticity causing systolic arrest takes place only in the inner layers of the muscles of the heart, because if by a special apparatus, digitoxin is applied only to the outer surface, then this organ shows the increase in pulse volume and the slowing of rate but stops in diastole instead of systole.

The increase in force of the frog's heart under digitoxin is sufficient alone to raise materially the blood pressure because if this organ is isolated and blood vessels are excluded by connecting it with a glass vascular system, the result is a marked rise of arterial tension.

In **warm-blooded animals** also, the main action of these substances is seen upon the heart. At first, the force of this organ and capacity for work is greatly increased, the rate is as a rule decreased, then with large doses the force is diminished, it becomes irregular and stops completely.

The action of digitoxin upon the **heart** may be divided into four stages. The first consists of an increase in the force of contraction due to direct stimulation of the cardiac muscle, usually

accompanied by a diminution in rate secondary to stimulation of the vagus, both centrally and peripherally. The blood pressure rises, chiefly as a result of this increased force of the muscle. The second stage consists of a further increase in force, but also of an increase in rate due to depression or exhaustion of the vagus. The blood pressure is still high. In the third stage the blood pressure is high, but irregular, as is also the pulse. This is due to beginning exhaustion of some cardiac fibres. In the fourth stage the blood pressure falls, accompanied by great irregularity in rate and force of the heart's contraction. In warm-blooded animals, the heart stops paralyzed in diastole, but as mentioned before in the cold-blooded, as the frog and turtle, it stops in systole.

The amount of **vagus** action varies considerably in different individuals. There are cases in human beings, especially in febrile conditions, when the stimulation of this nerve is not observed and the pulse is not slowed. On the contrary, others show a very strong stimulation of the pneumogastric, which may make the pulse dangerously slow.

Although the force of the pulse is raised by digitoxin in the presence of paralysis of the blood vessel walls, yet it is possible that under normal conditions the **vasomotor system** is stimulated centrally and peripherally and that this condition assists in the raising of the arterial tension. Digitoxin seems to contract at least temporarily the vessels of the limbs and of the splanchnic area. Digitalin and strophanthin seem to contract those of the splanchnic area only, but to dilate the vessels of the limbs and brain.

No increase in the flow of **urine** is seen after the use of the digitoxin series in normal human beings, but in dropsical conditions, especially those due to weakness of the heart, a great diuresis may be observed. *This diuresis is, therefore, not due to a direct action upon the renal epithelium, but rather to the increased circulation through the kidney incident to the rise in blood pressure.*

Few symptoms referable to the **central nervous system** are

observed during the action of small doses of digitoxin. The convulsions which occur near death after poisoning with digitalis are probably due in part to stimulation of the convulsive centre in the medulla, and in part to the asphyxia, which results from the failing circulation.

An exceedingly important action of the digitalis group is the **local irritant** one. This is sometimes so severe as to produce after internal administration, nausea, vomiting, diarrhœa with marked inflammation of the gastro-intestinal tract, and after subcutaneous injection, abscess and sloughing. The nausea and vomiting caused by the heart poisons is sometimes so distressing as to force the discontinuance of the internal administration in some cases of cardiac insufficiency.

Habit or tolerance is never noticed even after using digitalin, digitoxin or strophanthin for periods or months, and, with suitable doses the increase in the pulse volume and decrease in pulse rate are as obvious at the end as at the beginning of the period. On the other hand, if the dose has been rather large, evidences of **cumulative effects** may occur, as in the case of Prof. Koppe, who had taken on three successive days a large dose of digitoxin and who showed on the fourth day alarming symptoms of cardiac failure. Other less serious symptoms of overdoses or of cumulative effects are the following: irregularity of a previously regular pulse with quickening, also a feeling of pressure and pain around the heart, sometimes dizziness and specks before the eyes and a sensation of great weakness and dyspnœa. Marked delirium and hallucination sometimes occur and are probably due, as are most of the other symptoms, to disturbance of the circulation.

STROPHANTHIN has an action on the heart almost identical with that of the digitalis active principles.

It differs from digitoxin in dilating the vessels of the limbs and brain which are contracted by the former; but strophanthin like digitoxin also contracts those of the splanchnic area.

Recent work has shown that the action of strophanthin is much less certain by oral or subcutaneous than by intravenous admin-

istration because this glucoside is rapidly destroyed and excreted. In fact, Hatcher found that it took ten times the subcutaneous fatal dose when given by mouth to produce toxic symptoms in animals. Strophanthin has decided *local anesthetic* properties.

The other members of this group, as **Scillain, Convallamarin, Helleborin, Bufonin, Bufotalin, Erythrophlein,** etc., have practically the same qualitative action as digitoxin, digitalin, and digitalein. Erythrophlein has to a certain extent, local anæsthetic action.

SUMMARY OF GROUP ACTION.—*Intense stimulation of cardiac muscles causing increase in the force of the pulse and a rise of blood pressure, with medicinal doses. Depression of the heart muscle with irregularity, fall of blood pressure and death from cardiac failure with large toxic doses. Arrest of the heart in diastole in warm-blooded but in systole in cold-blooded animals. At first, stimulation of the vagus with slowing of pulse followed by the depression of this nerve and a quickened pulse. Marked local irritation sometimes leading to vomiting and diarrhœa after internal administration. Tremendous increase in the flow of urine in dropsical conditions due to uncompensated heart. Central nervous system but secondarily affected and action on these parts of but little importance in poisoning.*

THERAPEUTIC APPLICATION.—The indication par excellence for the use of the **heart tonics** is in conditions *where the heart is accomplishing an insufficient work and where the blood pressure is too low,* and the arteries improperly filled. The main use, therefore, is in the treatment of *cardiac diseases,* especially those of valvular origin, either stenosis or insufficiency.

Digitalis and allied substances are indicated in these conditions only when the heart is incapable of doing its normal work, and especially when such symptoms of incompetency as cyanosis, dyspnœa or dropsy are present. These drugs often have remarkable action in reducing the size of a *dilated heart,* and also in producing a compensatory hypertrophy. The diminution in the rate of the pulse should not be used alone as a

criterion of the good results of digitalis, for irritability of the vagus may be decreased from one cause or another. Then the pulse will not be decreased in rate, although the heart may be much strengthened and the dyspnœa, cyanosis and œdema may have disappeared, while the urine is increased in quantity.

In toxæmias where there is much *acute myocardial degeneration*, no good effects may be seen after the administration of members of the digitalis group. When compensatory hypertrophy is reached and when no symptoms of failing compensation are present, these substances are *contraindicated*. Great caution should be observed when much myocarditis is present, as these drugs may strain the heart and produce a sudden stoppage. They can be used with good effect in pericarditis and in conditions where the circulation through the lungs is impeded as in *phthisis*, *pneumonia* and *pleurisy*.

Great difficulty has been met in the past in obtaining a reliable digitalis preparation, since the leaves spoil rapidly, likewise the preparations made from them. Now a number of firms standardize their tinctures and fluidextracts. In Germany, the two most important standardized products have been Digalen and Digipuratum.

A few years ago, Fraenkel used and recommended intravenous injection of Strophanthin in the dose of one milligram in twenty-four hours. He and others showed series with strikingly good results.

MATERIA MEDICA.

Digitalis (U.S.P.), Digitalis Folia (B.P.), leaves of Digitalis Purpurea or Foxglove, contain the glucosides digitalin, digitalein, and digitophyllin, and the neutral body digitoxin, all of which possess the characteristic digitoxin action. Besides these, are present to a small extent two resins, one, toxiresin, derived from the decomposition of digitoxin and the other, digitaliresin, from that of digitalin. They do not act like digitoxin, but belong to the picrotoxin group. A member of the saponin group is also present in digitalis, *i. e.*, digitonin. The leaves which are official, contain mainly digitoxin, and digitophylline, while the seeds contain digitalin and digitalein.

Digitoxin is a neutral body soluble in alcohol, insoluble in water. It is absorbed with difficulty, but also excreted with difficulty so that its effects are cumulative. It is very irritant locally. **Dose:**—0.0001 G.

Digalen, special solution of amorphous digitoxin in water and glycerine. **Dose:**—1.0–2.0 c.c.

Digitalin and **Digitalein** are soluble in water. They are much weaker than digitoxin. Digitalin is decomposed in the stomach by the gastric juice, but it may be administered subcutaneously as it is not very irritating. **Dose:**—0.0002–0.0006 G.

Digitalin Verum, pure preparation of Digitalin. **Dose:**—0.0002–0.0005 G.

Tinctura Digitalis (U.S.P.,B.P.). **Dose:**—0.3–2.0 c.c. Br. (5–15 ♏). Average (U.S.P.) **1.0 c.c.**

Fluidextractum Digitalis (U.S.P.). **Dose:**—0.01–0.2 c.c. Average (U.S.P.) **0.05 c.c.**

Infusum Digitalis (U.S.P.). **Dose:**—4.0–16.0 c.c. Average (U.S.P.) **8.0 c.c.**

The tincture and fluidextract contain a larger percentage of digitoxin than the infusion because the latter is more easily extracted by alcohol.

Strophanthus (U.S.P.), seeds of Strophanthus Hispidus and Strophanthus Semina (B.P.), seeds of Strophanthus Kombe, containing the non-glucosidal bitter principle, strophanthin.

Tinctura Strophanthi (U.S.P.,B.P.). **Dose:**—0.1–0.6 c.c. Br. (5–15♏). Average (U.S.P.) **0.5 c.c.**

Strophanthinum-Thoms. cryst. glucoside obtained from Strophanthus gratus and identical with ouabain. Is colorless, soluble in hot water and 100 parts cold water, 30 parts alcohol. **Dose:**—By mouth, 0.003–0.025 G. intravenously, or intramuscularly 0.0005 G.

Scilla (U.S.P.,B.P.), Squills, bulbs of Urginea Maritima or Broom, containing the brown bitter glucoside scillain, insoluble in water, soluble in alcohol.

Tinctura Scillæ (U.S.P.,B.P.). **Dose:**—0.3–2.0 c.c. Br. (5–15 ♏). Average (U.S.P.) **1.0 c.c.**

Fluidextractum Scillæ (U.S.P.). **Dose:**—0.03–0.2 c.c. Average (U.S.P.) **0.1 c.c.**

Other members of the digitoxin group are the following substances:

Convallamarin, glucoside soluble in alcohol, extracted from the Convallaria Majalis or Lily of the Valley.

Helleborin, glucoside soluble in water, and Helleborein insoluble in water, both from Helleborus Niger.

Apocynein and Apocynin from Apocynum Cannabinum or Canadian Hemp.

Euonymin from Euonymus Atropurpureus.

Adonidin from Adonis Vernalis.

Antiarin from Antiaris or Upastree.

Neriin from Nerium or Oleander.

Thevetin from Thevetia.

Erythrophlein, the only alkaloid of this series. Extracted from bark of Erythrophlœum Guineense.

Epinephrin from suprarenal extract.

Bufonin and **Bufotalin** from toads' skins.

GROUP OF QUININE.

The group is composed of **QUININE** and other alkaloids extracted from the Cinchona bark. The characteristic action of its members is a *decrease of the functional activity of all forms of protoplasm;* the poisonous action being greater, the lower the scale of the protoplasm. On account of this selective action for lower organism, enough quinine may be given to a highly organized individual, such as man, which will not impair his vital functions but will attack a unicellular parasite in his blood, as the malarial protozoon. It is upon this fact that the greatest specific use of quinine in the treatment of malaria is based.

When fresh water **amœbæ** or infusoria are treated with a very weak solution of quinine, there is first, an exceedingly transient increase in their movements, followed rapidly by a decrease and complete arrest with granular degeneration of the protoplasm. When more quinine is used, the arrest of the movements and the granulation is immediate. A similar effect has also been observed upon leucocytes and upon the protozoa of malaria.

On account of the decrease in the movements of leucocytes, their passage through the walls of the blood vessels and the formation of **inflammatory exudates** may be checked. The number of leucocytes in the blood is also decreased. The **spleen** is diminished in size when pathologically enlarged in malarial fever.

In frogs, quinine produces, besides a condition of narcosis, some increased reflexes due to a preliminary stimulation of the cord. This is, however, followed by general paralysis of the whole central nervous system. This effect is not remarkable as it is usual with most protoplasmic destroyers, before the decrease in the functional activity and death of the tissues, that there should be a preceding stage of increased irritability. Also in the muscles of the frog there is to be observed, at first, an increased power of contraction and capacity for work but rapid tiring. The heart muscle never shows increased activity, but from the first, a decrease in force and ultimately complete arrest.

Corresponding to the destruction of the lower forms, there occurs a decrease in the **metabolism** of warm-blooded animals. The nitrogenous end products in the urine are diminished and the formation of heat is lessened. As a sequel of this action on metabolism, a **febrile temperature** may be lowered.

On account of its general action on protoplasm, quinine is a **local irritant.** When injected subcutaneously much pain is felt and sloughing occasionally occurs. Given by the mouth, it produces in small quantity, an increase in appetite and in the secretion of digestive juices, while in larger quantities, irritation and inflammation of the gastro-intestinal tract, with decreased appetite, nausea, vomiting and sometimes diarrhœa.

The highly organized protoplasm of the **central nervous system** of mammals is less affected than that of the lower forms. Yet in sufficient quantities the same depressant effect is to be observed. Sensation and consciousness are decreased and death is produced by paralysis of the respiratory centre and of the heart.

The rate of the **heart** beat is at first increased, probably through central depression of the vagus. In consequence of the increase in rate the blood pressure may be slightly raised. The cardiac muscles are soon affected, when both the rate and force of the circulation are decreased and the blood pressure falls, until the heart stops entirely.

Quinine in the form of the hydrochloride of quinine and urea produces marked local anæsthetic action similar to cocain. Even in strength of only ¼ to ½ per cent., the anæsthesia is more complete than with cocain and lasts much longer—even up to four to five days after subcutaneous injection. A fibrinous exudate is formed at the site of injection which, however, is not marked with low concentrations.

Quinine is rapidly **excreted** by the kidneys, partly as such, and partly as an oxidation product.

When this drug is given in large doses to an ordinary individual, or in moderate doses to a very susceptible human being, various symptoms called **untoward effects** occur. Among these are headaches, fullness in the head, dizziness, roaring in the ears,

disturbances of vision with partial or complete blindness, deafness, dulling of consciousness, sleepiness and even coma. These symptoms usually subside after the withdrawal of the drug, although blindness and deafness have lasted over quite a period of time. The aural disturbances are said to be due to congestion of the middle ear, while those of the eye are attributed to anæmia of the retina. Other symptoms, probably due to the irritant effect of quinine, are gastro-intestinal inflammation, skin eruptions and irritation of the kidneys. Bleeding from the latter and other mucous membranes may also occur. Abortion, which is said to have been seen after quinine, is probably due to both irritation of the gastro-intestinal tract and also to a stimulant action on the smooth muscles of the uterus, corresponding to the muscular stimulation observed in frogs.

The **other alkaloids of cinchona** possess an action closely resembling that of quinine, except that they have some tendency to produce increased reflex irritability and convulsions. They are all weaker, except **cinchonidine.**

SUMMARY OF GROUP ACTION.—*Protoplasmic poison causing arrest of movements, granular degeneration and death of lower forms. Specific poison to plasmodium of malaria. Depressant to movements of leucocytes, thus stops inflammatory exudates. Untoward effects on ears and eyes causing roaring in the ear, partial blindness and deafness, also skin eruption, gastro-intestinal disturbance and irritation of kidneys. Depressant to central nervous system and heart.*

THERAPEUTIC APPLICATION.—The main use of **quinine** is as a specific in the treatment of *malarial fever.* Its action is more marked on the young forms and in order to affect these most powerfully, it is usually administered in large doses a few hours before the division of the parasite which is coincident with the chill. Thus the blood is made to contain a maximum amount of the drug at the time of division. It is also employed as a preventative of malaria in districts where it is prevalent, but for this purpose only small doses are necessary.

It is used in the form of rectal injections in *amœbic dysen-*

tery, with the hope that it may destroy the protozoa of this affection as it does those of malaria.

Quinine is used as an antipyretic in *febrile diseases* other than malaria, such as typhoid fever, typhus, pneumonia, tuberculosis and septicæmia, but its *antipyretic action in such conditions is not as powerful as that of the coal tar preparations*, which have, in great measure, replaced it.

It has been used as an analgesic in *neuralgia* and *headache*. When these conditions are not of malarial origin, its good effects, if any, may be explained by the depressant action upon the central nervous system.

It is also employed in wasting diseases and convalescence from acute affections, as an *appetizer* because of its bitter taste, and as a *gastro-intestinal stimulant* to increase the digestion and absorption of food. For the last indication, the crude preparations of **cinchona** are usually administered before meals in an alcoholic beverage.

As a **local anæsthetic,** quinine and urea hydrochloride has risen in importance. It is usually injected in the strength of ¼ to 1 per cent. and applied to the mucous membrane in that of 10 per cent. to 20 per cent.

MATERIA MEDICA.

Cinchona (U.S.P.), bark of Cinchona Calisaya and other hybrid species, Cinchonæ Rubræ Cortex (B.P.), bark of Cinchona Succirubra. The Cinchonas grow in South America, India and Malay Isles. They contain in the native 1 per cent., in the cultivated 5 per cent. alkaloids. About half of this is quinine. The balance is composed of a variety of closely allied bodies, of which the principals are quinidine, cinchonine and cinchonidine.

Tinctura Cinchonæ (U.S.P.,B.P.). **Dose:**—0.5 c.c. Br. (½–1 fl.ʒ). Average (U.S.P.), **4.0 c.c.**

Tinctura Cinchonæ Composita (U.S.P.,B.P.). **Dose:**—4.0–15.0 c.c. Br. (½–1 fl.ʒ). Average (U.S.P.), **4.0 c.c.**

Vinum Quininæ (B.P.). **Dose:**—15.0–30.0 c.c. Br. (½–1 fl.ʒ).

Quinina (U.S.P.), a white, crystalline alkaloid, soluble in 1750 parts H_2O and in 0.6 part of alcohol. It forms crystallizable salts with an intensely bitter taste. The most commonly used are the sulphate, bisulphate and hydrochlorate. When given subcutaneously or intravenously, the last two are preferred on account of their greater solubility.

Dose of Quinine and all its salts 0.2–1.0 G.; Br. (1–10 grains). Average (U.S.P.), **0.25 G.** For malaria usually given in the dose of 1.0 G. about two hours before the expected chill and a few tenths at intervals during the

balance of the time. For amœbic dysentery given in the form of high enemata containing 0.1 per cent. quinine.

Quininæ Sulphas (U.S.P.,B.P.), soluble in 720 parts H_2O and 86 parts of alcohol. Contains 74 per cent. quinine.

Quininæ Bisulphas (U.S.P.), soluble in 8½ parts H_2O and 18 parts of alcohol. Contains 60 per cent. of quinine.

Quininæ Hydrochloridum (B.P.), soluble in 18 parts H_2O and 0.6 part alcohol.

Quininæ et Urea Hydrochloridum, soluble in about 1 part of H_2O. Suitable for subcutaneous injection, as a local anæsthetic in solutions of ¼ to 10%.

Euquinine, ethylester of quinine, said to possess therapeutic virtues of quinine without bitter taste. Dose same as quinine.

Aristoquinine, another artificial derivative of quinine, white, tasteless powder. Dose same as quinine.

GROUP OF ACETANILID AND PHENOL.

This group comprises chiefly bodies extracted from coal tar, their derivatives and synthetic products, besides certain substances obtained from wood tar and also some natural deposits having a resemblance to the first in composition and action.

The use of members of this series to reduce fever temperature dates back to the introduction of salicylic acid in 1875. This was followed by carbolic acid, resorcin, and various quinolin derivatives, which were discovered in an attempt to synthetize quinine. Each year, large numbers of synthetic compounds were made, with the aim at first of making quinine artificially, later of forming compounds which had the advantage of those already formed without their disadvantages.

All the members of this group have, in a general way, the same action as quinine. This is a depressant one on the lower forms of protoplasm and, therefore, they are **antiseptics,** *although they do not have a specific action upon the malarial plasmodium.*

They *decrease the body* **temperature** *in fevers.* This is due partly to diminished heat production, partly to increased heat dissipation brought about by a dilatation of the superficial blood vessels. On the contrary, the internal vessels are not dilated, so that there is not at first a fall of blood pressure, and in some cases there may even be a rise.

They all depress the **central nervous system,** *especially at first, the parts associated with the sensation of pain.* Later, the entire central nervous system is paralyzed producing unconsciousness, collapse and death due mainly to *paralysis of the respiratory centre in the medulla.* With many members of this group, there has been observed in animals a stage of increased irritability, which may lead to convulsions.

The **heart's** action may, at first, be increased in rhythm, but later it is decreased in both rate and force. The antipyretics often produce in large doses **methæmoglobinæmia.** They also give rise to **local irritation** which, after internal administration, may lead to vomiting, diarrhœa and gastro-enteritis, acute or chronic. This irritant action also occurs in the kidneys, where they are excreted partly changed.

The **untoward effects** which are sometimes observed are *excessive sweating, skin eruptions, chills, digestive troubles, irritation of the kidneys, buzzing in the ears, disturbances of vision, cyanosis and collapse.* The latter may even occur after very small doses of some of these substances.

According to the action of the members of this group they are indicated in therapeutics for three different purposes, firstly, as antipyretics, i. e., to lower febrile temperature; secondly, as analgesics to decrease pain; thirdly, as antiseptics. Some are used for one of these purposes, others for all three.

The different members of this large group vary enormously in toxicity as may be judged by the comparative dose of carbolic acid, 0.01 gramme and benzoic acid 1.0 gramme, i. e., one hundred times greater than the other. Regardless of the degree of toxicity, but making a purely arbitrary division based on the chief usage, the group is again subdivided into the Acetanilid Division used mainly to *reduce febrile temperature and quiet nervous pains* and the Phenol Division whose members are chiefly employed at the present time as *antiseptics and disinfectants* in different parts of the body. It is, however, to be remembered that the divisions are not at all sharp, that members of one frequently pass into the other.

ACETANILID DIVISION.

In this subdivision are described Acetanilid, Antipyrine, Salicylic Acid and other substances related to these.

ACETANILID, when administered by the stomach to dogs in doses of 0.5 gramme per kilo of body weight, produces somnolence and sleep, but when injected in this quantity into the blood-stream it causes convulsions and death due to paralysis of respiration. The **heart** does not suffer as much as the respiratory system.

Doses of a few grammes given to a normal man produce some pain in the stomach, sleepiness with occasional headaches, cyanosis and profuse sweating but little or no decrease of temperature, and at times even a slight elevation.

When given to febrile patients in even much smaller doses, the **temperature** rapidly decreases and all the attendant symptoms and distress of fever diminish or disappear; but in the course of a few hours, if a new dose is not given, it rises again. The rate of the pulse is lowered by the lowering of the temperature, as it rises again as soon as the latter becomes once more elevated.

Although in many cases no other symptoms but a fall of temperature and pulse and an increase in comfort occurs, yet in a certain percentage of patients, one or all of a train of symptoms may arise, so-called **untoward effects.** These consist of severe chills with clashing of teeth, profuse and exhausting sweats, nausea and vomiting, skin eruptions and cyanoses and in severer cases alarming collapse which has even resulted in death. Besides, there may occur certain brain symptoms as fullness in the head, headaches and roaring in the ears.

Occasionally acetanilid has been used, either with or without doctors' advice, as a dusting powder over chronic ulcers, especially of the varicose variety. In consequence of the long continued external application or of the internal ingestion in the form of "patent headache powders," there have been observed many cases of **chronic poisoning and habit.** In these cases the

patients complain that when they do not dust it on their ulcer, or in the other cases if they do not take the "powder," that they are uncomfortable, have headaches and general distress. Such patients have loss of appetite, gastro-intestinal disturbances, often marked anæmia, great general debility with special weakness of the heart, and more or less cyanotic appearance, especially of the lips and face. The cyanosis is due in part to changes in the blood coloring matter as it is to a certain extent transformed to methæmoglobin. The destruction of the red blood corpuscles which occurs produces the anæmia.

The **nitrogenous metabolism** as may be judged by the nitrogen in the urine is increased by small doses but is decreased by large ones. It might be inferred that larger doses by a depressing action on protoplasm lessen tissue changes.

The *decrease of temperature in fever is probably effected chiefly through the action of acetanilid upon the heat regulating centres* by narcotizing the same, thus preventing the stimulation from the toxins present in different febrile diseases. A considerable loss of temperature occurs from the dilatation of the superficial vessels of the skin while all the deeper ones remain contracted, with the *blood pressure as high* if not higher than before. Thus much blood is brought to the surface of the body and cooled.

Acetanilid does not decrease the phagocytic activity of the leucocytes nor does it decrease the production of antitoxin in an infectious disease. Its antiseptic action is not very powerful, requiring a strength of 2 to 5 per cent. and having no specific effect on the malarial parasite.

Excretion is rather rapid and takes place after partial oxidation through the kidneys which may at times show marked irritation.

Other aniline derivatives as **Phenacetine, Lactophenin, Methacetine, Exalgine** and **Benzanilid** have practically the same action as acetanilid. They are said to produce less often untoward symptoms, and Phenacetine and Lactophenin are reputed with more analgesic effect in neuralgic affections. The mother substance of all these, **Aniline,** is a very poisonous

product not used in medicine. It causes, in small doses, convulsions, cyanosis, vomiting and fatal collapse.

ANTIPYRIN is less poisonous than acetanilid, but its action is otherwise very much the same. It causes in animals the same decrease of consciousness, convulsions and collapse. In practice, however, *it produces less frequently the different untoward effects* and it does not attack the red blood corpuscles or change the hæmoglobin to methæmoglobin.

When applied locally to a mucous membrane, *it contracts the* **blood vessels** just like adrenaline, therefore the part becomes white and anæmic. If there is any hemorrhage, it arrests the same. In the nose it shrinks up the turbinate bodies thus allowing a better field for manipulations. It makes operations upon the eye, nose and throat less bloody, and also produces a considerable amount of *local anæsthesia.*

Some more phenylhydrazine derivatives are **Salipyrine, Resopyrine, Pyramidon, Pyrodine** and **Antithermin.** The first two act very much like antipyrin but the last three, Pyrodine, Antithermin and Pyramidon, are much more toxic and should be used only with great caution. Phenylhydrazine itself is a very poisonous substance producing a brown coloration of the blood due to methæmoglobin formation and also to a colored product of this drug. It causes severe depression of the central nervous system and death with convulsions.

Among the first antipyretics introduced in medicine were **QUINOLINE** and three of its derivatives **Kairin, Kairolin** and **Thalline.** Quinoline was introduced because it is present in the quinine molecule which has such wonderful effects on intermittent fever. Soon its use had to be discontinued as it produces so often and easily collapse. In small doses in animals, it causes sleepiness and loss of sensation, but larger quantities produce death from *paralysis of the medulla.* Kairin, kairolin and thalline were much less poisonous, yet their use has now been discontinued. More recently two new derivatives of quinoline, Analgen and Thermifugine, which are not very poisonous, have been introduced in practice.

SALICYLIC ACID and its simple salts such as Sodium Salicylate, have practically the same general action as acetanilid only less powerful. They are less apt to produce the disagreeable untoward symptoms but require much larger doses for antipyretic and analgesic effect.

Salicylic acid is a little stronger antiseptic than acetanilid. In sufficient concentration it *stops ferment action;* thus it arrests gastric and pancreatic digestion and stops the fermentation of sugar and alcohol. It also stops the movements of protozoa and leucocytes, like quinine, although it is not as powerful as the latter and does not act specifically in malaria. When applied to the skin in the form of very concentrated solutions or ointments, it *softens and removes the horny layers of the epidermis* but does not attack the deeper ones. In solid form, taken internally, it may produce reddening and superficial corrosion of the mucous membranes of the gastrointestinal tract, but these effects are never to be seen from diluted solutions or from the salts.

Salicylates increase the **nitrogenous metabolism** to the extent of ten to twenty per cent. after moderate doses. After large poisonous quantities, it may be decreased, as after acetanilid. The increase in the nitrogen output is not alone in the form of urea but also of uric acid, which may show an augmentation of nearly fifty per cent. Corresponding to this increased uric acid excretion, there is a marked leucocytosis in the blood.

The diminution of **febrile temperature** is less than with antipyrin, but it requires much larger doses of salicylic acid to produce **toxic symptoms in animals.** These consist of vomiting, somnolence, at first increased pulse and respiration, but later decrease in both, convulsive respirations, convulsions, paralysis, especially of the hind legs and death in collapse. With small doses the superficial blood vessels alone are dilated and the **blood pressure** is raised just as with acetanilid.

The **untoward effects** which occasionally occur in man consist of *profuse sweating, chills, buzzing in the ears, partial or com-*

plete deafness, dimness of vision, skin eruptions, vomiting, headache and dizziness.

The salicylates are **excreted** *chiefly by the kidneys*, partly as such, and partly changed to salicyluric acid, a compound with glycocoll. In passing through these organs, they may produce, with small doses, and on account of their irritant action, increase in the flow of urine, but with large doses and weak kidneys, albuminuria, hæmaturia, and even acute Bright's disease.

There is a small amount of salicylic acid *excreted by the milk, perspiration, synovial secretion of joints and bile.* The excretion by the sweat may explain the skin eruptions, while that by the joints the good effects observed in acute rheumatism, and that by the liver, the stimulation of this organ and the increased flow of both the solid and fluid constituents of bile.

Increased bleeding at the menstrual period and occasionally abortions have followed the salicylate treatment, also hemorrhages from other organs, such as the gums and nose, have been observed.

Recently, different products of salicylic acid have been made artificially. These are insoluble in water and are therefore insoluble in the stomach and less irritating to this organ, but they are dissolved or decomposed by the alkaline pancreatic juice. They may then become absorbed and produce the same general action as the mother substance. In the case of one of these bodies, **SALOL,** it is decomposed into salicylic and carbolic acid so that it has the action of both substances. Other similar derivatives which do not give off free phenol are **Salophen, Aspirin, Novaspirin, Salocoll, Malakin** and **Salocreol.** Plant life gives us two bodies of this group, **Methyl Salicylate** or oil of wintergreen, and the glucoside **Salicin,** which is decomposed into salicylic alcohol; both of these have the characteristic action of this division. Oil of wintergreen is more irritant locally than salicylic acid because it possesses in addition to its characteristic action, the irritant effect of all volatile oils.

PHENOL DIVISION.

This subdivision contains the members of the group which are used in clinical medicine nowadays almost exclusively for antiseptic purposes. It consists of different phenols, as Carbolic Acid and Thymol, Creosote, Naphthalene and its derivatives, Benzoic Acid and Ichthyol.

PHENOL.—The general protoplasmic effect seen from most of the members of the coal tar group, is especially well marked with phenol or carbolic acid. The latter stops the movements of protozoa and leucocytes, arrests the development and even kills the lower plant forms, as bacteria. Like most of the other protoplasmic poisons it shows a much greater toxic action on the lower animal cells as protozoa and spermatozoa, etc., than on the bacteria. Its degree of **antiseptic action** varies enormously with different organisms; for instance, the ordinary pus cocci are killed by a low concentration, while anthrax spores and tubercle bacilli require a long exposure of a five per cent. solution for any effect at all.

Phenol precipitates the proteids both in solution and in animal tissues. If applied to the **skin** in concentrated form, it at first burns, but this sensation soon passes away with paralysis of the sensory nerve endings and the skin *becomes anæsthetic* and turns white due to the precipitated albumen of the cells. In a few days the scab falls off and the brown stain remains for a little while. On account of this precipitation of albumen the caustic effect as a rule remains limited to the upper layers if the application has been of short duration. On the contrary, when phenol has remained in contact with tissues for a few days, as has happened after the use of concentrated carbolic acid poultice on a finger, deep protoplasmic necrosis and **gangrene** of the member may be observed. Local anæsthesia and allay of itching may take place from very diluted solutions which have no corrosive effects, so that this action is a direct one on the sensory nerve endings.

When a very large dose of carbolic acid is taken by a man, he

may, as after hydrocyanic acid, drop to the ground unconscious and die within a few minutes from paralysis of the vital functions without any convulsions or other symptoms, for the *toxic effect on the central nervous system and heart is very great.* With smaller doses, a train of symptoms is to be observed, which consist of nausea, vomiting, great weakness, headache, dizziness, somnolence, disturbance of the intellect, muscular twitching and convulsions, great weakness of the heart and dyspnœic respirations and at last death in collapse. There is usually marked sweating, salivation and increased bronchial secretion. The latter may give rise to a cough.

A form of general poisoning, not infrequently results from absorption by the skin or wounds when applied as a remedy. It takes the form of great general weakness, headaches and somnolence, very weak pulse, sometimes œdema, diminution in the secretion of urine, and a dark brown or black color of this secretion, which may also contain albumin and blood.

In frogs, there is to be seen at first, general depression of movements, then muscular twitchings, strychnine-like convulsions and lastly general paralysis. In warm-blooded animals, the **heart** and **respiration** show a slight increase at first, then both functions are decreased, the heart muscle being directly paralyzed, likewise the respiratory centre.

The red **blood corpuscles** are to a certain extent destroyed, but there is no transformation of hæmoglobin to methæmoglobin except outside the body. The central nervous system shows the same change as from acetanilid only much more strikingly. It consists of a general paralysis preceded by stimulation of certain areas, especially those producing convulsions. Its action on the **metabolism** and **febrile temperature** is of the same order and, in fact, it was used formerly as an antipyretic.

In its passage through the body, phenol at first *combines with glycuronic and sulphonic acids* and the resulting compounds are much less toxic. When these are exhausted, it then circulates as such and by oxidation yields hydroquinon and pyrocatechin. All of these are excreted by the urine, and the last

two impart to this secretion the dark brown or black color seen in cases of poisoning. The color always intensifies by exposure to the air because of further oxidation. The **kidneys** as a rule suffer from more or less irritation, and at times a true nephritis with albumen, blood and casts is produced. After prolonged administration, fatty degeneration of liver cells has been observed and corresponds to the protoplasmic poisonous action.

PYROGALLOL or pyrogallic acid, a trioxybenzol, produces practically the same symptoms as phenol, only in a much stronger degree and, in addition, destroys the red blood corpuscles and *changes the hæmoglobin to methæmoglobin.* It also produces *destructive changes in the liver and kidneys.* It is so poisonous that it is even *dangerous in extensive external application to the skin.* It colors the latter a deep brown, a stain which can be removed by benzine.

RESORCINE, another phenol, dioxybenzol, acts on warm-blooded animals very much like carbolic acid but less powerfully. It is, however, even more strongly antiseptic. It is excreted in the urine in the same way.

CREOLIN contains different cresols and is supposed to be less poisonous than carbolic acid, but of the three cresols, metacresol is the only one which is less poisonous, the para- and orthocresols being more toxic than carbolic. All have in general the same action, and external application of creolin has resulted in the same poisoning as from the group type. There is a saponified solution of creolin, called lysol, with identical action.

THYMOL, another phenol, acts like the latter but being very insoluble in water, does not become absorbed readily, therefore is much less toxic to warm-blooded animals. Its antiseptic powers are considerably greater and it has especially well-marked effects upon intestinal parasites, more particularly the "hook worm." In **chronic poisoning** it causes degeneration of the protoplasm of parenchymatous organs like phenol. It is *excreted by the urine conjugated with sulphonic and glycuronic acid* and is very apt to irritate the kidneys.

CREOSOTE is a mixture of phenols obtained from wood tar.

It has as strong antiseptic action, but is less toxic to warm-blooded animals than carbolic acid.

NAPHTHOLS, when injected in large doses into animals, produce practically the same symptoms as the phenols, yet they are less apt to give rise to convulsions. They are much stronger germicides. Given in smaller doses over a period of time, they produce diarrhœa, with severe irritation and degeneration of the kidneys, leading to nephritis. Another great characteristic symptom, is a form of degeneration of the retina, optic nerve and lens. Plaques of opacity are seen in the retina and lens. These symptoms may be also observed in man. The naphthols become excreted in the urine combined with glycuronic and sulphonic acid. Naphthalene is easily oxidized in the body to naphthols and acts like the latter.

BENZOIC ACID possesses the general action of this subdivision only the poisonous symptoms are elicited with immensely larger doses than with carbolic acid. Its irritant action, and that of its salts, is especially well marked, being very prone to produce nausea and vomiting. It augments the **nitrogen excretion** like salicylic acid, but contrary to the latter, *decreases the excretion of uric acid.* Benzoic acid is excreted, partly as such, partly combined with glycocoll in the form of hippuric acid, by the urine where it acts as an **antiseptic** and **irritant.** Small amounts have also been found in the saliva of dogs.

TAR contains different antiseptic members of this division and has a weak but similar effect on the organism.

ICHTHYOL, a tarry product of fossil fishes, contains also different antiseptic compounds and in a very mild degree has some of the action of this group.

SUMMARY OF GROUP ACTION.—*Contained in the first pages of Group of Acetanilid and Phenol.*

THERAPEUTIC APPLICATION.—Members of the **acetanilid subdivision** are used chiefly to *reduce febrile temperature in different fevers other than malaria.* In the latter, although they may decrease the temperature, they do not exercise a specific action on the malarial parasite.

The decrease of febrile temperature is sought, either when the latter becomes dangerously high or when there is marked discomfort from it. The drugs of this group are usually given in small doses every three or four hours when the fever is high. The difference of influence on different fevers varies a little; for instance, they depress less markedly fevers from septic infection and pneumonia. They are very active in typhoid fever, in the eruptive diseases as scarlet fever, measles and in certain febrile cases of tuberculosis.

On account of their depressant effect on the sensory side of the central nervous system they are employed to check *headaches* and *neuralgic pains*. Some, such as **salicylic acid** and its compounds, are used in the treatment of *acute rheumatism*. The effect may be antiseptic on the affected joints or the improvement may be due to the antipyretic and analgesic actions combined. It does not seem that the course of the disease or that the frequency of complication is at all shortened. Salicylic acid and some of its compounds have been used externally in the form of ointments as *antiseptics and irritants in different skin diseases* and also internally as *disinfectants of the gastro-intestinal tracts*.

The members of the **carbolic acid group** are *also used both internally and externally as antiseptics*. The different skin diseases make the chief field for all these substances applied in the form of washes, ointments, collodia, etc. **Carbolic acid, creolin** and **lysol** are used very extensively for *washing wounds* and surgeons' hands. **Thymol** has found its chief field of usefulness in the treatment of the *hookworm disease*, and **benzoic acid** as a *urinary antiseptic*.

MATERIA MEDICA.

(A) Aniline Derivatives.

Aniline, amido-benzol, is not used in medicine because of its great tendency to produce collapse.

Acetanilidum (U.S.P.,B.P.) (antifebrine), white, almost tasteless crystals, permanent in air, soluble in about 180 parts water, soluble in alcohol, ether and chloroform. Best administered, as a powder. It produces a fall of temperature one hour after administration which may last for 12 hours. Used to decrease temperature in infectious fevers, as typhoid, measles, scarlatina, acute articular rheumatism and tuberculosis. As an analgesic it

is used in tabes dorsalis, neuralgia, migrain and headaches. As an antiseptic it is sometimes dusted on ulcers and wounds. **Dose:**—0.2–0.5, up to 4.0 G. in 24 hours. Br. (1–3 grains). Average (U.S.P.) **0.25 G.**

Exalgine (methyl antifebrine), white, crystalline body, slightly soluble in water, soluble in alcohol, ether and chloroform. Same uses as acetanilid. **Dose:**—0.2–0.5 G. up to 4.0 G. in 24 hours.

Antisepsine (para-brom-acetanilid), colorless crystals, soluble in alcohol, insoluble in water. Used externally as an antiseptic in the form of dusting powder and salve.

Acetphenetidinum (U.S.P.), Phenacetinum (B.P.), colorless, odorless, tasteless crystals, almost insoluble in water, soluble in alcohol. It has the same uses as acetanilid, but it is a more efficacious analgesic. **Dose:**—0.2–0.5 G. Average (U.S.P.) **0.5 G.**

Methacetine contains one less methyl group than phenacetine. It is more easily soluble in water and is used in the same doses and for the same indications.

Benzanilid resembles phenacetine and is used in small doses for children. Same dose as the above.

Lactophenyl resembles phenacetine in properties, action and uses. Same dose as the above.

(B) Antipyrine Series.

Antipyrina (U.S.P.), Phenozonum (B.P.), white crystals without odor, with slightly bitter taste, freely soluble in water, alcohol and chloroform. Used locally to relieve congestion and stop hemorrhage during operative procedures upon the nose, throat and eye and internally as an antipyretic and analgesic. Rather smaller doses can be used for analgesic purposes. **Dose:**—0.5–1.0 G. up to 8.0 G. in 24 hours. Br. (5–20 grains). Average (U.S.P.) **0.5.**

Salipyrine, compound of salicylic acid and antipyrine, white powder soluble in about 200 parts water, very soluble in alcohol and chloroform. Same action and uses as antipyrine.

Resopyrine, compound of resorcine and antipyrine. Same action and uses as antipyrine. **Dose:**—0.5–1.0 G.

Pyrodine (acetyl phenyl hydrazine), colorless crystals, soluble in alcohol, much more poisonous than antipyrine. **Dose:**—0.01–0.06 G.

Antithermine (phenyl hydrazine levulinic acid), also more dangerous than antipyrine.

Pyramidon (dimethyl amido antipyrine), white tasteless powder soluble in water. Same uses as antipyrine. **Dose:**—0.2–0.5 G.

(C) Quinoline Series.

Quinoline, colorless liquid which smells like tobacco, soluble in water. It acts as a base, and therefore forms salts with acid. Its salts were used internally as antipyretics, but were afterwards discarded because of their danger. Now it is sometimes used as a disinfectant gargle for diseases of the throat in the strength of 1–500%.

Kairin, Kairolin and Thalline, are quinoline derivatives which were formerly extensively used as antipyretics. **Dose:**—0.1–0.2 G.

Analgen, a recent quinoline derivative composed of white crystals, in-

soluble in water, soluble in alcohol. Used in fevers, neuralgias and headaches. **Dose:**—0.5–1.0 G.

Crurin Purum (quinoline bismuth sulphocyanate), fine, reddish, crystalline powder, insoluble in water, used externally as a dusting powder over wounds.

Chinosol (oxyquinoline sulphonate of potassium). Yellow crystals with astringent taste and saffron odor, easily soluble in water but insoluble in alcohol. Strong antiseptic and hemostatic. Used internally for tuberculosis and externally as disinfectant in solution of 1–1000, also in 5–10 per cent. in ointment and as dusting powder. **Dose:**—1.0 G. daily.

(D) Salicylic Acid Series.

Acidum Salicylicum (U.S.P., B.P.), white crystalline body, soluble in about 300 parts water. **Dose:**—1.0 up to 4.0 G. per day. Br. (5–30 grains). Average (U.S.P.) **0.5 G.**

Sodii Salicylas (U.S.P.,B.P.), white crystals odorless with a sweetish taste, soluble in about 1 part of water. Solutions turn red on standing. **Dose:**—1.0 up to 15.0 G. per day. Br. (10–30 grains). Average (U.S.P.) **1.0 G.**

Lithii Salicylas (U.S.P.), deliquescent white crystals, very soluble in water. **Dose:**—1.0 up to 15.0 G. per day. Average (U.S.P.) **1.0 G.**

Oleum Gaultheriæ (U.S.P.), oil of wintergreen, yellowish fluid with characteristic odor and taste. Soluble in alcohol, insoluble in water. Composed of 90 per cent. methyl salicylate. **Dose:**—0.3–1.0 c.c. Average (U.S.P.) **1.0 c.c.**

Spiritus Gaultheriæ (U.S.P.), 5 per cent. alcoholic solution of the oil. **Dose:**—1.0 to 6.0 c.c. Average (U.S.P.) **2.0 c.c.**

Salicinum (U.S.P., B.P.), glucoside found in willows and poplars. It is composed of white crystals with a bitter taste, soluble in 21 parts of water, decomposed by a ferment into salicyl alcohol and glucose. **Dose:**—0.5 to 2.0 G. Br. (5–30 grains). Average (U.S.P.) **1.0 G.**

Phenylis Salicylas (U.S.P.), or Salol, white crystals, aromatic odor, almost tasteless, insoluble in water. Decomposed by alkaline fluids of the intestines into phenol and salicylic acid.

It has no action on the stomach because it remains insoluble in acid juices and so it can be used to coat pills destined for intestinal action. In the intestines, it acts like its constituents as an antiseptic, and after absorption, as an antipyretic. It is used as an internal antiseptic in inflammatory conditions of the intestines. It is also employed as an antipyretic in feverish conditions such as colds, influenza and rheumatism. It is used for diagnostic purposes to determine the motor efficiency of the stomach, for when salicyluric acid appears in the urine it is an indication that the salol has passed from the stomach into the intestines. **Dose:**—0.5–2.0 G. Br. (5–30 grains). Average (U.S.P.) **0.5 G.**

Salophen (acetyl-amido-phenol salicylic acid), has the same action and uses as salol, but it is less poisonous because instead of free phenol the non-poisonous acetyl-amido-phenol is liberated in the intestines. **Dose:**—0.3 to 1.0 G.

Salocoll (phenocoll salicylate), is also split in the small intestines into salicylic acid. Same dose and uses as salol.

Malakin.—Another compound similar to salol. Same dose and uses.

Aspirin, acetyl salicylic acid, almost entirely insoluble in water and only dissolved in the intestines, where it is split into salicylic acid. **Dose:**—1.0–2.0 G.

Mesotan (methoxymethylester of salicylic acid), greenish liquid almost odorless, and easily absorbed by the skin. Used in articular rheumatism rubbed into the skin in 5 c.c. doses.

Salicylic acid and its derivatives are used internally and externally as antiseptics, internally, as antipyretics and analgesics, especially in acute articular rheumatism, the salicylates are given in gramme doses every hour until the pain and fever are relieved, or until poisonous or untoward symptoms arise.

The preparations of salicylic acid should not be administered after buzzing in the ears ensues. They should not be given to menstruating women, as they may increase the hemorrhage from the uterus.

(E) Phenol Series.

Phenol (U.S.P.), Acidum Carbolicum (B.P.), colorless, deliquescent crystals, which become pink on standing and melt at 40° C., very volatile and liquefy when mixed with five parts of water. Soluble in water enough to make a 5 per cent. solution. It is used nowadays as an internal antiseptic in pill form, but was formerly employed as a febrifuge. Its main application is as an external antiseptic in 5 per cent. solution over wounds, ulcers and so forth, also to disinfect wounds and for antiseptic douches. On account of its local anæsthetic action it is sometimes used in itching skin diseases as a wash. **Dose:**—0.01–0.05 G. up to 0.5 in 24 hours. Br. ($\frac{1}{6}$ to 1 grain). Average (U.S.P.) **0.065.**

Unguentum Phenolis—3 per cent.

Glyceritum Phenolis—20 per cent.

Aseptol, or sozolic acid, a 33 per cent. solution of ortho-phenol sulphonic acid, brown syrupy liquid which smells like phenol, but is less poisonous and less irritant than the latter. It is used for the same purposes externally.

Sodii Phenolsulphonas, colorless crystals without odor, saline taste, soluble in 5 parts water. **Dose:**—0.3 to 1.0 G. U.S.P., **0.25 G.**

Zinci Phenolsulphonas, colorless efflorescent crystals, very soluble in water and alcohol. Used as external antiseptic in $\frac{1}{2}$ to 2 per cent. solution in the treatment of gonorrhea and ulcerative processes. **Dose:**—U.S.P., **0.125 G.**

Resorcinol (U.S.P.) (meta-dioxybenzol), or resorcine colorless crystals, very soluble in one part water.

Formerly used as an antipyretic; now only as an internal and external antiseptic. It is very irritant and even a caustic in concentrated solution, and, therefore, is best used in the strength of 1 to 2 per cent. It is employed to disinfect the gastro-intestinal tract, the vagina, the urethra and rectum. **Dose:**—0.3 to 6.0 G. up to 3.0 G. in 24 hours. Average (U.S.P.) **0.125 G.**

Pyrogallol (U.S.P.) or pyrogallic acid, light or colorless crystals which quickly darken upon exposure to light. It is very soluble in water and acts as a strong reducing agent.

Although it is never used internally, cases of poisoning arise from its absorption by the skin after external application. These results forbid the application of this substance over large areas of the skin and other absorbing surfaces. It is used as a stimulant and antiseptic in skin diseases, especially in psoriasis in 5 per cent. to 10 per cent. solution and is best applied to the

spots in the form of collodion. It produces a brown stain which can be removed by benzine. On account of this brown coloration it is sometimes used to dye hair. In 20 per cent. solution it is used as a caustic.

Lenigallol, or pyrogallol triacetate, substitute of pyrogallic acid used in the form of 20 per cent. ointment in skin diseases.

Eugallol (pyrogallol monoacetate). Same use as the above.

Thymol (U.S.P.,B.P.), obtained from the leaves and tops of Thymus Vulgaris; it is a white crystalline body, almost insoluble in water, but soluble in alcohol, ether, chloroform and oils. It is also liquefied when rubbed with chloral, camphor, menthol and phenol. **Dose:**—0.05–0.2 G. Br. (½–3 grains). Average (U.S.P.) **0.125 G.**

Thymolis Iodidum, reddish-yellow powder, insoluble in water and glycerine, slightly soluble in alcohol, easily soluble in ether, chloroform, collodion, fixed or volatile oils. Used externally as an antiseptic dusting powder, also in ointments, suppositories and in solution in liquid petrolatum 10 per cent. as a spray.

(F) Creosote Series.

This series contains a variety of phenol derivatives obtained by the distillation of wood tar, especially that obtained from beech.

Creosotum (U.S.P.,B.P.), clear, oily liquid with a smoky odor, containing some of the higher phenols, but not carbolic acid. It is less poisonous than carbolic acid, but it possesses also antiseptic and antipyretic properties. It is now mainly used as an internal antiseptic and also in the treatment of phthisis. Given in capsule or emulsion. **Dose:**—0.2–1.0 c.c. in 24 hours. Br. (1–5 ♏). Average (U.S.P.) **0.2 c.c.**

Creosotal (creosote carbonate), clear, thick, amber-colored liquid, insoluble in water, soluble in alcohol. It contains 90 per cent. creosote. Same action and uses as creosote. **Dose:**—0.2 up to 1.0 c.c. in 24 hours.

Guaiacol, liquid closely related chemically and pharmacologically to creosote, but it is said to be more poisonous than the latter. Same uses as creosote. **Dose:**—0.2 up to 1.0 G. in 24 hours.

Duotal (guaiacol carbonate), white crystals insoluble in water, soluble in alcohol. Used for the same purposes as creosote. **Dose:**—0.2 G. up to 1.0 G. in 24 hours.

Benzosol (benzoyl guaiacol), white crystals, same use as previous preparations. **Dose:—0.2 G.**

Cresol (U.S.P.), straw colored liquid with aromatic odor soluble in 60 parts water, miscible with alcohol and glycerine in all proportions. Composed of three cresols. An excellent external antiseptic. **Dose:**—Average (U.S.P.) **0.5 c.c.**

Creolin, impure preparation of the above, brown liquid, insoluble in water, but forming a milky mixture with the latter. It contains various cresols, pyridine bases, and resins, obtained from coal tar. Used as an external antiseptic in the strength of 1 to 2 per cent. solution.

Lysol is a preparation of creolin made transparent and soluble in water by boiling with alkalies. It makes a soapy solution with water. Uses same as cresol and creolin. It has the advantage over creolin that instruments placed in its solution may be readily seen on account of its transparency.

Europhen (isobutyl ortho-cresol iodide), yellow, odorless, insoluble powder used to dust on wounds as an antiseptic.

(G) Pyridin Series.

Pyridin, colorless liquid with a peculiar odor, very soluble in water, alcohol and ether. Occasionally used by inhalation in dyspnœa and asthma.

Iodolum (tetraiod-pyrrol) yellow powder, odorless, tasteless, almost insoluble in water. Contains 90 per cent. iodine. Used externally as an antiseptic dusting powder. Internally, as a substitute for iodide of potassium in syphilis. **Dose:**—0.03–0.5 G.

Menthol Iodol. Dose:—0.03–0.5 G.

(H) Naphthalene Series.

Naphthalenum (U.S.P.), hydrocarbon obtained from coal tar. It consists of volatile, colorless, shining crystals with the odor of coal tar and an aromatic taste. Insoluble in water, soluble in 15 parts of alcohol, in ether and oils.

It is used as an internal disinfectant in intestinal catarrh, in dysentery and tuberculosis of the intestines. Also as external antiseptic in scabies in a 10 per cent. ointment. **Dose:**—0.05–0.5 G. up to 6.0 G. in 24 hours. Average (U.S.P.) **0.125 G.**

Betanaphthol (U.S.P.), **Naphthol** (B.P.), white crystal, soluble in about 1000 parts of water, very soluble in alcohol and ether. Used for the same purposes as naphthalene. For skin eruptions it is sometimes employed in a 5 per cent. solution. **Dose:**—0.05 to 0.5 G. Br. (3–10 grains). Average (U.S.P.) **0.25 G.**

Asaprol (calcium sulphonate derivative of naphthol). It is a white powder soluble in water and alcohol. It is eliminated by the kidneys which it may irritate as naphthalene and naphthol. Same use as naphthalene. **Dose:**—0.1–1.0 G.

Epicarin (naphthol and toluic acid derivative), yellow powder, soluble in alcohol, ether, and oils. Used as naphthol for scabies in form of ointment. Said to be non-poisonous.

(I) Benzoic Acid Series.

Acidum Benzoicum (U.S.P.,B.P.), white crystals, aromatic odor, soluble in alcohol and ether, soluble in about 300 parts water; forms crystallizable salts with the alkalies. **Dose:**—1.0–4.0 G. up to 10.0 G. in 24 hours. Br. (8–15 grains). Average (U.S.P.) **0.5.**

Sodii Benzoas (U.S.P.,B.P.), white crystals soluble in 2 parts of water. **Dose:**—1–4 G. Br. (8–30 grains). Average (U.S.P.) **1.0 G.**

Lithii Benzoas (U.S.P.), white crystals, soluble in 3 parts of water. **Dose** same as the above.

Ammonii Benzoas (U.S.P.,B.P.), white crystals, soluble in 5 parts water. **Dose** same as the above.

These substances are used chiefly as expectorants and antiseptics of the bronchial and urinary tracts. They are seldom used now as intestinal antiseptics.

(J) Tar Series.

Pix Liquida (U.S.P.,B.P.), or tar, is a thick brown, syrupy liquid obtained by the dry distillation of pine wood. It consists of a mixture of phenols, cresols and naphthalenes. **Dose:**—Average (U.S.P.) **0.5 G.**

Oleum Picis Liquidæ, oil distilled from tar. **Dose:**—Average (U.S.P.) 0.2 c.c.

Syrupus Picis Liquidæ. Dose:—5.0 to 15.0 c.c. Average (U.S.P.) 4.0 c.c.

Unguenti Picis Liquidæ.

Anthrasol, or colorless tar, is a decolorized preparation of tar.

These various tar preparations are used externally in the form of ointments for the treatment of skin disease where they act as antiseptics and irritants by virtue of their constituents.

(K) Ichthyol Series.

Ichthyolum is the ammonium salts of sulphonic acids obtained by distilling bituminous deposits of fossil fishes found in Tyrol. It is a viscous, reddish-brown liquid, with a bituminous odor and taste, soluble in water, glycerine and fats.

It can be given internally as an antipyretic and disinfectant of the gastro-intestinal tract, but its chief use in confined to the treatment of skin diseases in the form of an ointment containing 5 to 50 per cent. **Dose:**—0.5 to 1.0 c.c.

Thiolum is an artificial substitute for ichthyol made by sulphonating hydrocarbon of soft coal. It is used very much in the same way as ichthyol.

Ichthalbin (compound of ichthyol and albumin). It is used mainly internally as a disinfectant of the gastro-intestinal tract. **Dose:**—0.5 to 1.0 G.

(L) Chrysarobin Series.

Chrysarobinum (U.S.P.,B.P.), is a yellow powder extracted from Goa which is present as an exudation in the lacunæ of the trunks of the Brazilian tree Andira Araroba. It is present to the extent of 75 per cent. in Goa powder, together with chrysophanic acid. It is difficultly soluble in water, but it mixes well with oils and fats. In solution in caustic alkalies, it becomes changed by the air to chrysophanic acid.

It is used externally only as an irritant, antiseptic and antiparasitic in the treatment of skin diseases, and especially in psoriasis and tænia as a 5 per cent. ointment or collodion. The black stains which it produces on the skin can be removed by benzine.

PART II.

In this section are to be found a few heterogeneous series of substances of animal origin which cannot easily be grouped elsewhere. Among these are the digestive ferments, the secretions and extracts from organs and the artificial foods.

GROUP OF DIGESTIVE FERMENTS.

This first subdivision contains the digestive ferments which have been used in diseases of the gastro-intestinal tract to replace those which are lacking. They are of the three varieties *proteolytic, amylopsic and steapsic:* the chief ones are pepsin, pancreatin, papain, and different diastases.

PEPSIN digests proteids in acid media, best in solutions of 0.2 per cent. hydrochloric acid. It does not act in an alkaline reaction, but is even destroyed in a very short time by alkaline carbonates.

Since pepsin or its antecedent, pepsinogen, is almost never absent from the stomach contents, except in complete atrophy of the mucous membrane or in extensive cancer, its use is indicated practically only in these two conditions. In catarrhal processes of the stomach, pepsin is usually present, but inactive on account of the great diminution or absence of hydrochloric acid. Under these circumstances, not pepsin, but hydrochloric acid is indicated to render active the pepsinogen which is already present.

PANCREATIN differs from pepsin in that it digests proteids in neutral and alkaline solution and is destroyed by 0.2 per cent. hydrochloric acid. Its only possible use is in cases of decreased pancreatic secretion, or where the gastric secretion is totally stopped, so that pancreatic, instead of gastric digestion, might be carried on in the stomach.

The presence of **proteolytic enzymes** in the vegetable kingdom is quite widespread. We find them in the common pineapples, in figs, in the insect-eating plant Drosera and in the Brazilian plant, Carica Papaya. The enzyme found in the last mentioned plant, papain, is the only one used practically in medicine.

PAPAIN, or papayotin or papoid, digests proteids in alkaline, neutral, and acid solutions. It has been employed instead of pepsin or pancreatin to help gastric or pancreatic digestion. It has also been used to digest croupous or diphtheritic membranes in the throat.

DIASTASE is the enzyme of malt which changes starches into sugar. There is also an amylolytic ferment called **Taka-diastase,** present in Eurotium Oryzæ, as aspergillus. Neither Diastase nor Taka-Diastase has any utility in medicine, as starch digestion is almost never at fault. The **alcoholic malt extracts,** which are usually sold, have no starch digestive properties because the alcohol prevents the action of ferments.

SUMMARY OF GROUP ACTION.—*Digestion of the various food stuffs in different reactions according to the ferment.*

MATERIA MEDICA.

Pepsinum (U.S.P., B.P.), proteolytic ferment obtained from the stomachs of pigs, which should be capable of digesting not less than 3,000 times its weight of freshly coagulated egg albumin. It is a white, almost odorless powder with a slightly bitter taste, soluble in about 100 parts of water, but more soluble in acidulated water. **Dose:**—1.0–5.0 G. Average (U.S.P.) **0.25 G.**

Pancreatinum (U.S.P.), a mixture of the enzymes present in the pancreas of warm-blooded animals, usually obtained from the pig. As a rule it contains in the active state only the proteolytic and the starch splitting ferments, but not the fat splitting ones. It is a yellowish, white powder, with a slight odor and taste, slowly soluble in water. **Dose:**—1.0–5.0 G. Average (U.S.P.) **0.5 G.**

Liquor Pancreatis (B.P.), solution of ferment of pancreatic glands. **Dose:**—1–2 ʒ.

GROUP OF BILE.

BILE of different animals was used empirically in the treatment of diseases by the ancients. It is, however, only recently

that its pharmacological action has been studied and that rational indications for its use have been found.

The bile acids or their salts are undoubtedly the chief active ingredients. When injected subcutaneously or intravenously into animals, bile or bile salts produce a depression of the **heart** and **central nervous system** and *decompose the red blood corpuscles*. These symptoms are very similar to those observed in jaundice in human beings.

When given by the mouth, they increase the peristalsis of the intestines and the absorption of fats, and decrease intestinal putrefaction. They are *absorbed by the stomach and intestines and are carried to the liver where they are in chief part* **re-excreted.** During their passage through the liver, they greatly stimulate this organ and *increase the total secretion and the absolute quantity of acids and other solids of the bile*, out of proportion to the actual quantity of bile or bile salts administered.

The **laxative effect** is probably due to the irritation caused by the increased amount of free taurocholic and glycocholic acids in the intestines. The **antiseptic action** results from the more rapid onward movements of the intestinal contents and from the special antiseptic action of free taurocholic acid. The **increased absorption of fat** is a sequence of their better saponification and emulsification and of stimulation of the absorptive powers of the intestinal mucosa.

The main **uses** of bile are in the treatment of constipation and of conditions when the digestion and absorption of fats are impaired, and as a cholagogue.

SUMMARY OF GROUP ACTION.—*Special stimulant action upon the liver causing great increase in both solid and watery constituents of bile. Laxative and internal antiseptic. Depressive effect upon the circulation and destruction of the red blood corpuscles.*

MATERIA MEDICA.

Fel Bovis Purificatum (U.S.P.), Fel Bovinum Purificatum (B.P.), is formed from the fresh bile by the addition of alcohol, filtration and evaporation to a pasty consistency. It is best prescribed in pills coated with salol to prevent action and absorption in the stomach. **Dose:**—0.3–2.0 G. Br. (8–15 grains). Average (U.S.P.) **0.5 G.**

GROUP OF ADRENALIN.

When extracts of the suprarenal gland or its active principle, **ADRENALIN,*** are injected **intravenously,** changes in the circulation resembling those produced by the digitalis group are to be observed. At first the force of the heart's contraction is strengthened, its rate is decreased and the blood pressure is elevated. Later this organ becomes irregular and weakened. The increase in the force of the **heart** is due to stimulation of its muscles, while the slowing is the result of stimulation of the pneumogastric nerves. The increase in the blood pressure is due to the augmented force of the heart plus contraction of the **peripheral vessels.** This contraction of the vessels is due to local action upon the vaso-constrictor endings.

These symptoms differ from those produced by digitalis, as they are of exceedingly short duration; also because the vascular effect is infinitely more marked than that on the heart muscle and is the chief feature in the rise of blood pressure with suprarenal extract. It seems that the contraction of blood vessels is not uniform throughout the body and that those of the splanchnic area are the chief ones affected. This influence is of but short duration after a single dose, for the blood pressure may return to normal in a few minutes. The shortness of action is explained by the rapid decomposition of the active principle.

After often repeated intravenous injections of suprarenal extract over a prolonged period of time, *arteriosclerotic conditions* in the aorta may be produced which lead to necrosis of the media with deposits of calcium salts.

When applied locally to a **mucous membrane,** adrenalin *contracts the blood vessels,* and makes it white and bloodless; thus, a congested conjunctiva, or swollen turbinate bodies, may be immediately blanched and shrunken. If there is local hemorrhage it may be stopped by this powerful, local, contractile effect on the vessels.

Other nerve endings in smooth muscles than those in blood

* Also called Epinephrin and Suprarenin.

vessels are also affected. Those in the walls of the bladder, stomach and intestines are relaxed, while those of the uterus, vagina, vas deferens, seminal vesicles and external genitalia are contracted. In the eye, besides contracting the blood vessels, suprarenal extract or adrenalin dilates the **pupil** by stimulating the dilator fibers supplied by the superior cervical ganglion. They do not act on the muscles supplied by the oculomotor nerve.

Adrenalin stimulates the protoplasm of the **secreting glands,** just like physostigmin, and this increases the secretions of the saliva, of the mucus in the throat and of the sweat.

After hypodermic injections of large doses in animals, the **central nervous system** is at first stimulated, but later depressed followed by death from *respiratory failure*. *Hemorrhages* from the **kidneys** and mucous membranes are sometimes observed.

The **sugar metabolism** is altered after subcutaneous administration so that the percentage of sugar in the blood is increased and glycæmia and glycosuria are produced. This is due to the specific liberating effect which adrenalin has on the stored sugar. Thus the blood is flooded with more than can be temporarily oxidized. After internal administration no action is discernible because adrenalin is probably decomposed before absorption.

SUMMARY OF GROUP ACTION.—*Powerful stimulation of smooth muscle fibers especially in the walls of blood vessels, thus arresting local hemorrhage and congestion and raising blood pressure by injection into the circulation. Also, some stimulant action on the heart. No action by internal administration, and fleeting effect even by intravenous injection because of ease of decomposition of the active principle.*

THERAPEUTIC APPLICATION.—Extracts of **suprarenal glands** and solutions of **adrenalin** have been employed chiefly on account of their constricting influence on blood vessels, to *arrest hemorrhage*, and *relieve the congestion* of the mucous membranes of the nose, throat and eyes, as in nasal catarrh, hay fever, pharyngitis, and conjunctivitis. They have also been employed to *prevent hemorrhage* during surgical operations on the nose and throat.

Their employment as a *stimulant to the circulation* in shock is objectionable on account of the very fleeting action of the principle.

Suprarenal extracts have been used, although with little benefit, in the treatment of Addison's disease, a sickness attended with destruction of the suprarenal glands.

MATERIA MEDICA.

Glandulæ Suprarenales Siccæ (U.S.P.), cleaned, dried and powdered glands of sheep and ox. Light, yellowish amorphous powder, partly soluble in water. **Dose:**—Average (U.S.P.) **0.25 G.**

Adrenalinum Hydrochloridum, white crystalline body, soluble in water, used in solution of 1–1000 to 1–10,000 for local application to mucous membranes. This body has also been called epinephrine, suprarenin, adrin, adnephrin, suprarenalin, etc., and has been prepared by various firms in standard solutions.

GROUP OF IODOTHYRIN.

The **THYROID GLAND** of animals and its active principle **IODOTHYRIN** produce marked changes in the **metabolism.** These consist of a great *diminution of weight due to an increase in the burning up of the body tissues; at first, of the fats alone, later, also of the proteids.* The increased destruction of the latter gives rise to augmentation of the urea in the urine. The **urine** is also greatly increased in quantity, as are also most of its solid constituents. Occasionally albuminuria and glycosuria occur.

The **heart** is rendered more rapid and the blood pressure is lowered; thus, overdoses produce palpitations, weakness and collapse.

The **nervous system** is also affected so that we may have headache, nervousness and tremors.

Occasionally symptoms of **gastro-enteritis** may be observed. The intensity of these symptoms varies greatly in different individuals. Patients suffering from exophthalmic goitre and myxœdema are especially sensitive. All the symptoms of exophthalmic goitre are aggravated by continuous use of thyroid preparations, but with **myxœdema** the reverse is true, if small increasing doses are used. In this disease the mucoid œdema gradually

disappears. The hair grows again and becomes less dry. The heart increases in rate and the urine in quantity. The intellect becomes brighter and the patient in due time becomes entirely normal. If, however, the use of thyroid preparations is discontinued in this disease, its symptoms gradually reappear. On account of these facts, it has been supposed that myxœdema is due to a decrease or absence of the normal secretion of the thyroid gland, while exophthalmic goitre is due to an overproduction of the secretion of this gland.

SUMMARY OF GROUP ACTION.—*Marked influence on metabolism causing an increased burning up of first fats, then proteids, thus reducing body weight. Specific curative action on myxœdema and conditions where there is an insufficiency of thyroid secretion. Depression of heart and central nervous system from large doses.*

THERAPEUTIC APPLICATION.—The main use of **thyroid** preparations is in the treatment of conditions where the normal thyroid secretion is thought to be decreased, as in *myxœdema, cachexia strumipriva, cretinism* and *common goitre.* Small doses should be given at first to learn the susceptibility of the patient in myxœdema and cachexia strumipriva (thyroid gland removed by operation). Then it should be continued throughout life. It is also sometimes of great value in *reducing obesity,* but in the obese it should be used with care for fear of reducing the weight too rapidly and causing undesirable symptoms. The urine should be carefully watched and when more nitrogen is excreted than is taken in by the food, it should be discontinued.

A tendency toward sugar in the urine from the use of thyroid in obesity, should make one especially cautious in examining the urinary secretion often.

MATERIA MEDICA.

Thyroid Gland of the sheep contains the proteid thyreoglobulin, which, by digestion, is decomposed into globulin and iodothyrin. The fresh gland may be administered raw or slightly broiled. Begin with one-quarter or one-half a gland per day.

Glandulæ Thyroideæ Siccæ (U.S.P.). Dried glands of sheep, yellowish powder, partly soluble in water. **Dose:**—Average (U.S.P.) **0.25 G.**

Thyroideum Siccum (B.P.), a powder prepared from the fresh thyroid

gland of the sheep. It is a light brownish powder with a meat-like odor. **Dose:**—2–10 grains in 24 hours.

Other preparations of thyroid are tablets containing 0.12 G. of the dried gland prepared by Parke, Davis; another tablet called Thyraden, 0.25 G. of the dried gland, prepared by Knoll and a preparation called "Iodothyrin" containing lactose and the same amount of iodine as the gland prepared by Bayer.

Iodothyrin is a white body almost insoluble in alcohol and water, containing less than 10 per cent. iodine, which possesses the same action as the crude gland and is probably its active ingredient.

HORMONES.

Since Sterling demonstrated the stimulant action which certain bodies in the living organs normally exert on various secretions, an attempt has been made to place one of these in practical application. This one is the hormone which produces increased peristalsis and was called by Zueltzer **HORMONAL.** It has been used successfully by this author and others in the treatment of constipation. It is administered subcutaneously every few days. Its action lasts for several days.

OTHER ANIMAL EXTRACTS.

Extracts of other organs, as thymus gland, testicles, ovaries, spleen, bone marrow and pituitary bodies, have been tried in therapeutics without much more than psychical effects.

Thymus gland contains a principle which lowers blood pressure and causes death by collapse, when given in very large quantities. It has been recommended in exophthalmic goitre, but without much effect.

Testicular extract was first recommended by Brown-Séquard as a rejuvenator and has been used more or less since, although without any apparent effect. Pöhl introduced instead of testicular extract, an alkaloid spermin isolated from testicles, and claims for it marked action in improving the metabolism in neurasthenia and other conditions.

Ovarian extract has been recommended for conditions of disturbed metabolism occurring in women at the menopause or in undeveloped girls.

Spleen and bone marrow extracts have been employed in different blood diseases, especially pernicious anæmia, on the theory that they might increase the blood-forming elements of the bone marrow and spleen. These have likewise been without results.

Pituitary extract has been recommended in acromegaly on the theory that the disease is due to a diminution of that gland.

TOXINES, ANTITOXINES, VACCINES.

TOXINES are a class of poisons of a highly complex, chemical composition and sometimes partaking of the albuminoid nature. They are found widely distributed, especially in the lower plant life as bacteria, but also in higher plants, as in the castor-bean or ricinus, the jequirity, common croton tiglium, etc. They occur in animal organisms, especially as the product of bacterial action under pathological conditions, and some of the most serious diseases of animal life are due to these products of bacterial activity. Among the many such, may be cited diphtheria, tetanus, typhoid fever, bubonic plague, cholera, etc.

Some of these toxines produce a pharmacological action not very different from that of some well-known drugs. Thus tetanus toxine produces the same tetanic convulsions which are observed after strychnine or its allies. Nevertheless, the mode of action differs considerably, because these substances act in immeasurably small amounts, and in suitable conditions, they tend to stimulate the formation in animal organisms of chemical substances foreign to these, which have the power of combining chemically with the toxines and rendering these innocuous. These are called **ANTITOXINES.** Some of the toxines when administered in small amounts have the power of stimulating the phagocytic activity of living cells towards the bacteria which have produced that toxine. Furthermore, they may stimulate the power of the living cells to actively destroy the toxines.

After many infectious diseases, the living organism loses the power of contracting the same disease again for a varying time of

from a few weeks, or a few years, to a complete lifetime. Thus syphilis and several of the exanthemata are generally accepted not to recur during the lifetime of an individual. This protection is called acquired immunity, and the principle is used in therapeutics in order to prevent diseases. It is called **vaccination** and was first introduced in connection with small-pox, when variolization was employed. The principle has been to diminish the virulence of the germs and thus the intensity of the inoculated disease. The first attempt at attenuation was practised by Jenner, when he immunized human beings against small-pox, by the use of the allied but much less virulent cow-pox. Since that time many other vaccinations have been introduced, and among the most successful may be mentioned that against rabies. More recently favorable results have been obtained by vaccination against typhoid fever and bubonic plague.

Occasionally, after the use of some antitoxic serum, as that of diphtheria, sudden death has occurred in man and in experimental animals. Researches on this point have shown that certain highly complex bodies, as albumins and albuminoids, have the power diametrically opposite to immunizing, i. e., they sensitize the organism in which they are introduced. Thus horse-serum may be given in considerable doses without ill effects to a guinea-pig who has never received an injection of this substance previously. When, however, a dose even so small as $\frac{1}{1000}$ of the original innocuous one is administered some days, weeks or even months later, the animal dies suddenly with symptoms of respiratory failure. At autopsy the cause of death is found to be spasmodic contraction of the bronchiole. This phenomenon of sensitization is known as **ANAPHYLAXIS.**

DIPHTHERIA ANTITOXINE.

Diphtheria antitoxine is obtained by immunizing horses with diphtheria. This is done by gradually injecting increasing doses of the diphtheria toxine. The serum obtained is titrated in strength with known toxines and is standardized in the term of units.

The standardized serum is injected both in cases of existing diphtheria and also as a prophylactic measure to those who come in contact with infectious foci, as physicians, nurses and family of the afflicted. The results obtained since its introduction by Roux have been astounding. In the Boston City Hospital, prior to 1895, the mortality from diphtheria was 46 per cent., while in five subsequent years after the introduction of the antitoxine, the mortality dropped to 12 per cent.

TETANUS ANTITOXINE.

This antitoxine has not given as favorable results as that of diphtheria, probably chiefly because the toxines of tetanus travel from the wound to the central nervous system by way of the nerves, while the antitoxine follows the lymphatic and blood channels and finds great difficulty in penetrating nerve tissue. Nevertheless, if the antitoxine is administered before convulsions occur, it may produce a certain prophylactic action.

SERUM OF CEREBRO-SPINAL MENINGITIS.

During the last few years great advance has been made in the serum treatment of cerebro-spinal meningitis, and from different countries, reports of great reduction in death-rate are published. The serum is injected intradurally and is believed to act by stimulating the phagocytes in destroying the cocci and their endotoxines.

SNAKE-VENOM ANTITOXINES.

Calmette, working with the venom of cobra and other poisonous snakes, was able to produce antitoxines which protect animals against the toxines present in these venoms. There is considerable difficulty in applying these to human beings.

ANTITHYROID SERUM.

The principle of antitoxine has also been applied to the correction of autointoxication from excess of some internal secretion.

Lately serum obtained from thyroidectomized goats and from other sources, has been employed, with a certain degree of success, in detoxicating the system from excess of the thyroid secretion in the disease Exophthalmic Goitre.

ARTIFICIAL FOODS.

Artificial foods have been prepared for cases of malnutrition where an insufficient amount of ordinary food is taken. We have among the proteid variety innumerable proprietary preparations of albumen, albumoses and peptones, some nucleo-proteids containing phosphorus, also carbohydrate preparations, especially represented by the infant foods and malted milks, and lastly, different preparations of fats, the oldest being cod liver oil.

These preparations have no particular superiority over the natural foods and, on the contrary, are often unpalatable, which in itself would make them less digestible. Thus, preparations of albumen, albumoses and peptones have seldom any advantage over properly prepared eggs or meat, proprietary foods for infants and invalids over common cereals, as tapioca, arrowroot or rice, and lastly, fat preparations or cod liver oil over cream, butter, olive oil or the fats in eggs or meat.

PART III.

This part contains drugs which are used in medicine chiefly for their local effects and, in fact, although most of them have a general action, it is the local one which is of greater prominence. It includes not only those substances which affect the place of application but also the place of excretion. Thus, with the division of urinary antiseptics, it is for local effect at the place of excretion, i. e., urinary tract, that these substances are used.

All the members of this part have local irritant action with the exception of some in the section of mechanical agents. Although we have attempted a classification according to the most common therapeutic application, yet the members of one group could easily be described in another from a purely pharmacological standpoint. The volatile oils used as urinary disinfectants present very nearly the same qualitative action as those described under skin irritants, and croton oil, given under purgatives, could be appropriately grouped with the skin irritant toxicodendrol.

SKIN IRRITANTS.

Almost all foreign substances which penetrate into the skin cause irritation, e. g., volatile bodies are irritants because they diffuse easily through the skin. Heat and cold are irritants of different intensity, depending on how much the rise or lowering of temperature departs from that of the body. Thus with these we may have all degrees of inflammation from redness to gangrene. Many drugs, when taken internally, such as iodides, bromides and mercury, may produce irritation of the skin, which is due either to an excretion of the medicine or its product by the same, or to a congestion of the vessels due to central action.

In this section we include only those drugs whose chief action is *irritation* by local application.

The irritation of the skin due to any drug always takes the form of ordinary skin inflammations of different grades, depending on the strength and quantity of the irritant, upon the susceptibility of the person and upon the place of application. Thus, poison ivy may, under some conditions, only produce an erythema, while under other circumstances it may give rise to papules, blisters, pustules and even ulcers. The subjective symptoms vary according to the intensity of action, as itching, burning or pain.

Besides the purely local action upon the skin, these irritants also influence in a reflex manner certain internal functions. Therefore *mild skin irritation produces an increase in the force, depth, or frequency of respiration. It also increases the force of the heart beat* resulting in a rise of blood pressure. Very *severe skin irritation over a large area* produces the reversed condition, i. e., a *decrease in the efficiency of the respiratory centre and heart with a fall of blood pressure*, e. g., a condition of collapse such as is seen after extensive burns.

The **metabolism** is increased by mild or moderate irritation of the skin so that we have an increased excretion of nitrogen and carbon dioxide.

The internal **temperature** is said to rise after mild dermal irritations and to fall after severe ones. The former is due to increase in metabolism, the latter to collapse. In fever, however, skin irritation may materially lower the body temperature by changing the distribution of the blood. Since in moderation it contracts the internal blood vessels and dilates the superficial ones, the hot blood is brought to the surface and cooled. The effect of cold baths in fever is a double one, producing a lowering of temperature by contact with cold and also by leaving the superficial blood vessels dilated after the bath. The influence of alcohol sponging is on the same order.

The skin irritants also affect the **local circulation of organs.** They are said to increase the circulation in parts directly under

the skin to which they are applied, but to decrease it in organs lying deeply beneath the same, *counter-irritation*. Thus, if applied to the chest they would produce hyperæmia of the intercostal muscles, but anæmia of the lungs.

For convenience of description, the skin irritants are divided into three groups, according to whether the action is due to the volatility of a substance, to the volatility plus special irritant properties, or to special irritant properties of a non-volatile body.

GROUP OF TURPENTINE OIL.

The action of this group is possessed by all volatile substances which are easily diffusible, such as the volatile oil of plants, including the oils of turpentine, cajuput, eucalyptus and arnica, sabine, juniper, cubeb, etc., and the artificial volatile hydrocarbons of the fatty acid series and their derivatives, including chloroform, ether and alcohol. Yet we restrict ourselves here to the description of the volatile oils found in plants which are chiefly composed of hydrocarbons, called *terpenes*.

These substances, on account of their easy diffusibility, *produce their local effects almost immediately after application*. This is never very severe, unless much of the substance is kept in contact with the skin for a long time, because they escape quickly by evaporation. For this reason also their action is of short duration.

The irritation as a rule consists only of a feeling of warmth, itching and redness. Because of the ease with which they penetrate protoplasm, they all have antiseptic action which varies somewhat with the different members, turpentine being one of the most active. When the volatile oils are taken *internally in small doses*, they produce a feeling of warmth in the stomach and often eructation of gas. They undoubtedly increase the movements of the upper gastro-intestinal tract. They also produce a hyperæmia of these parts and may increase the absorption of food stuff and also the glandular secretions. Another factor may act in this respect, i. e., the odor and taste of the pleasant volatile oils, which in a psychical way may improve the digestion;

in this way we probably can explain the good effects of after-dinner cordials. The leucocytes of the blood are also increased by the volatile oils.

When taken *internally in large quantities*, as, for instance, sabine which has been used to produce abortion, they cause severe gastro-enteritis with nausea, vomiting, and diarrhœa, intense pains and colic, great weakness of the heart and respiration, bloody and albuminous urine, even anuria and death in collapse.

They are **excreted** by the urine partly as such, partly oxidized and partly in combination with glycuronic acid. Large amounts passing through the kidneys produce intense nephritis, but with small quantities there may be observed only an aromatic odor and a slight increase in the urinary secretion. The latter is more or less antiseptic and it is on this account that a few oils, as that of cubeb, copaiba and sandalwood, are used as urinary disinfectants.

When injected into animals, there is usually to be observed a stage of increase in the **cerebral** and **medullary functions,** i. e., greater excitement and increase in respiration and blood pressure. Only with a few, as *oil of absinthe*, the cord is markedly stimulated and even convulsions may be observed. After the stage of stimulation, the entire nervous system becomes paralyzed and death takes place from failure of respiration.

Very little is known about the chronic action of volatile oils except that the regular and too copious drinking of cordials may lead to hyperacidity and other disturbances of the stomach. In the case of absinthe, however, there occur very frequently, insanity and epilepsy in the habitués which may be accounted for by the action of the volatile oil on the brain.

GROUP OF MUSTARD OIL.

When both black and white mustard are treated with water, there develops in each a different volatile oil, that of the former having specific irritant properties besides those due to its volatility.

The **OIL OF BLACK MUSTARD** being volatile, acts very rapidly but much more intensely than the essential oils of the previous division because it has specific irritant properties. It also acts much more deeply than the members of the next division which are non-volatile, and the inflammation caused by the former is more difficult to cure than that of the latter. The degree of irritation depends upon the concentration, length of exposure, etc., and may vary from simple *erythema to vesication, pustulation and even formation of ulcers.*

Taken **internally** in small quantities, mustard acts as a condiment and increases the appetite and digestion, but in cases where the stomach is hypersensitive, as in hyperacidity, it may produce burning and distress. In large quantities it acts as a powerful emetic.

Mustard plasters do not cause irritation rapidly because the oil has to be gradually formed from its antecedents by the moisture of the skin before they can act.

GROUP OF CANTHARIDIN.

This division includes the *non-volatile substances having special irritant properties.* The chief members are the active principles of Spanish flies, of poison ivy and poison oak, of cayenne pepper and of kaschew.

As these substances are non-volatile and not easily absorbed by the skin, the irritation comes on much later than with the members of the previous division, but it is of longer duration, because of the slow elimination.

CANTHARIDIN, the active principle of Spanish flies, produces very severe but less painful skin irritation than mustard oil because it is not volatile and does not penetrate so deeply. When taken **internally,** it causes intense burning and pain in the mouth, œsophagus, stomach and bowels. The colics may be excruciating. If taken in solution, blisters may be observed in the mouth and throat and the pain in the œsophagus may be so severe as to prevent deglutition. Violent vomiting and purging, pain

in the bladder, inability to pass urine (the little that is passed is albuminous and bloody), dyspnœic respirations, convulsions and death in collapse are the chief symptoms of poisoning in man.

As may be observed, the symptoms in man are dependent on the *frightful local irritation of the gastro-intestinal and urinary tracts*. They are also due to the action on the central nervous system, which consists of paralysis of the vital centres. Cantharidin is **excreted** by the kidneys.

The **susceptibility** of cantharidin towards different animals varies enormously; thus in the hen and hedgehogs large quantities may be taken without much effect, while in the rabbit a small dose, as in man, will produce intense symptoms of poisoning.

Capsaicin, mezerein and **euphorbin** have much the same action as cantharidin.

When extracts of **POISON IVY** or solutions of its active alkaloid are applied to the **skin,** or when persons are accidentally poisoned by the plants, a feeling of warmth and itching develops in from twenty-four hours to eight days after exposure. In a few hours an erythema appears, quickly succeeded by papules. In many areas these are replaced by small blisters and even large blebs, which may leave ulcerations. These skin lesions are accompanied by more or less œdema, which is, however, only well marked on the face and genitals (testicles and penis), which as a rule show few other lesions, but the œdema there is of great intensity, swelling the face to twice its normal size, completely occluding the eyes by enormously swollen lids. The most intense symptoms may last from three to six days, then they abate, and the skin returns to normal condition, after having peeled.

The main features of the **treatment of such poisoning** consists of scrubbing the affected parts with soap and water in order to remove the active principle. The application of the alcoholic solution of lead acetate is also of value by precipitating the active ingredients. The use of fatty substances is contraindicated because they have a tendency to dissolve and spread the poison.

After **internal administration** *symptoms of gastro-intestinal and renal irritation* are to be seen, just as with cantharidin.

The oil **CARDOL,** obtained from the Jamaican Kaschew, produces exactly the same effects. A case of cardol poisoning is indistinguishable from one of poison ivy.

SUMMARY OF GROUP ACTION.—*Irritation of the skin at the place of application and also of the kidneys where excreted. Taken internally gastro-intestinal tract much irritated. Action on the central nervous system of secondary importance.*

THERAPEUTIC APPLICATION.—Skin irritants are sometimes painted over *ulcers* to improve the circulation and hasten the repair, as for instance in the form of tincture of **myrrh.**

They are used to decrease *pain* reflexly, in the form of mustard and **cantharides** plasters for pain in the chest, **turpentine** stupes for the abdomen and counterirritant liniments for inflamed joints. Tincture of Cantharides is frequently put in hair restorers to stimulate the growth of hair.

They are applied on the skin over deep-seated *exudations* or *transudations*, such as water on the knee. Formerly they were much employed in the form of plasters to decrease inflammation of the deep-seated organs, as the lungs, stomach, intestines, etc.

Mustard, pepper and capsicum are used in small doses, as *gastric stimulants* to improve digestion and appetite. In large quantities mustard is given as an *emetic.*

On account of their irritant action and disinfectant properties, turpentine and terpene hydrate are sometimes of value as *expectorants* and bronchial antiseptics.

Cantharides was formerly used in small doses as a *diuretic* and by the laity to produce sexual excitement. The internal administration of this substance is exceedingly dangerous on account of its marked poisonous effect; the majority of the recorded cases of poisoning have resulted from this mode of application. Oil of sabine has been used chiefly illegitimately as an abortifacient and is of interest from the number of cases of poisoning resulting from this employment.

MATERIA MEDICA OF SKIN IRRITANTS.

Turpentine Division.

Terebinthina (U.S.P.). Thus Americanum (B.P.), concrete oleoresin from Pinus Palustris, composed of yellowish, opaque, crumbly masses. **Dose:**—1.0–4.0 G. Br. (15–45 grains).

Oleum Terebinthinæ (U.S.P., B.P.), obtained by distilling the above. **Dose:**—0.2–2.0 c.c. Br. (5 ♏–4 ʒ). Average (U.S.P.) **1.0 c.c.**

Resina or Rosin, residue after the distillation of turpentine. Used to make plasters.

Terpini Hydras (U.S.P.), rhombic crystals, soluble in 250 parts H_2O and 10 parts alcohol. **Dose:**—0.1–1.0 G. Average (U.S.P.) **0.125 G.**

Terebenum (U.S.P., B.P.), colorless liquid with a turpentine-like odor. **Dose:**—0.3–1.0 c.c. Br. (5–15 ♏). Average (U.S.P.) **0.5 c.c.**

Oleum Eucalypti, volatile oil obtained by the distillation of Eucalyptus Globulus.

Eucalyptol (U.S.P.), chief constituent of the oil of eucalyptus. It is a colorless liquid with an aromatic odor, soluble in alcohol and insoluble in water. **Dose:**—0.3–1.0 G. Average (U.S.P.) **0.3 G.**

Oleum Cajuputi, volatile oil obtained from Cajuputi Virideflora.

Oleum Arnica, volatile oil from Arnica Montana.

Oleum Sabinæ, volatile oil from Juniperus Sabina.

Mustard Division.

Sinapis Alba (U.S.P.), Sinapis Albæ Semina (B.P.), the dried seeds of Brassica Alba. This contains the glucoside sinalbine and the ferment myrosin. In the presence of water myrosin decomposes sinalbine with the formation of oil of mustard, sinapine and glucose.

Sinapis Nigra (U.S.P.), Sinapis Nigræ Semina (B.P.), the dried seeds of Brassica Nigra. It contains the glucoside sinigrin and the ferment myrosin. The latter decomposes sinigrin in the presence of water into allylisosulphocyanate of potassium, or the volatile oil of mustard and glucose.

Charta Sinapis (U.S.P., B.P.), paper treated with extracts of mustard.

Linimentum Sinapis Compositum contains the volatile oil of mustard, mezereum and camphor.

Thiosinamine, formed from volatile oil of black mustard, has been recommended to remove scars.

Fibrinolysin, solution of double salt of Thiosinamine with sodium salicylate, containing 15 per cent. of the double salt. Used instead of thiosinamine by subcutaneous, intravenous or intramuscular injection to remove scar tissue from various parts of the body.

Cantharides Division.

Cantharis (U.S.P., B.P.) consists of the dried beetles Cantharis Vesicatoria or Spanish fly. It contains cantharidin, an acid anhydride formed of colorless crystals, soluble in alcohol, ether, chloroform and slightly soluble in H_2O.

Ceratum Cantharidis (U.S.P.).

Collodium Cantharidatum (U.S.P.).

Tinctura Cantharidis (U.S.P., B.P.). **Dose:**—0.05–0.5 c.c. Br. (1–5 ♏). Average (U.S.P.), **0.3 c.c.**

Mezereum (U.S.P.), Mezerei Cortex (B.P.), bark of Daphne Mezereum which contains the irritant resin, mezerein, besides the glucoside daphnine.
Fluidextractum Mezerei. **Dose:**—0.05–0.5.
Capsicum (U.S.P.,B.P.), fruit of Capsicum Fastigiatum, a plant of Central and South America. It contains the oleoresin, capsicol, and the crystalline capsaicin.
Tinctura Capsici (U.S.P.). **Dose:**—0.5–4.0. Average (U.S.P.) **0.3 c.c.**
Emplastrum Capsici (U.S.P.).

URINARY ANTISEPTICS.

GROUP OF SANDALWOOD AND CUBEB OILS.

The volatile oils of **CUBEB, COPAIBA, SANDALWOOD** and **JUNIPER** are closely related chemically and pharmacologically. They are terpene derivatives and differ in no essential points from the other volatile oils described under skin irritants, so that the general pharmacological action of volatile oils also applies to this division.

They are **excreted** in part by the bronchi, but *chiefly by the kidneys* in combination with glycuronic acid. Not all of the oil is combined with the latter; a part is excreted unchanged, while another portion is transformed into an oxidation product before excretion. They have a certain amount of **local irritant action** which makes itself evident at the points of absorption and excretion, but these substances are a little less irritant than other volatile oils and with small doses are less apt to produce violent gastro-intestinal disorders. The oil of sandalwood seems to produce less irritation than those of cubeb and copaiba.

The medical administration of these bodies is not infrequently accompanied by pain in the stomach with dyspeptic and enteric **symptoms,** and also by pain in the back, over the bladder and in the urethra after micturition. When large doses are ingested, severe nausea, vomiting and diarrhœa may ensue; the urine may become albuminous, bloody, and diminished in quantity on account of the irritation of the kidneys.

After the administration of cubeb and copaiba, an eruption of the skin may occur. This **rash** takes the form of an erythema, papules or urticarial weals and is usually not accompanied by

fever. The skin may break out even after smoking cubebs, as is frequently done by laymen in certain parts of the country as a cure for catarrh of the air-passages. Sometimes symptoms of cerebral disturbance have been observed after large doses of cubebs.

During their passage through the **kidneys,** these substances stimulate the secretory structures and in medicinal doses may increase the renal secretion. They also *delay the decomposition and putrefaction so that the urine may remain clear for several days after it is passed* and when it does become cloudy, there are few or no putrefactive bacteria. On account of their excretion in combination with glycuronic acid by the urine, they may give the Fehling reduction and thus simulate the presence of sugar.

By virtue of their partial excretion through the **bronchial mucous membranes,** they stimulate its secretion and act also in this place as disinfectants.

The presence of albumin may be shammed in the nitric acid test by the **RESINS** present in the crude preparation of cubeb and copaiba, because they give rise to a precipitate. These resins are possessed of an action very similar to, but much less powerful than, that of the oils upon the urinary and gastro-intestinal tracts.

BUCHU may be placed in this group because it contains a volatile oil which has much the same action as those of cubeb and copaiba. **UVA URSI** or bearberry contains certain glucosides called arbutin and methylarbutin, which are excreted by the urine partly unchanged and partly transformed to hydroquinones. These bodies may give to the urinary secretion a smoky color, especially on standing, when the unchanged arbutin may become decomposed by the bacteria. Just as the oils mentioned above, but not in so marked a manner, uva ursi acts as a *genito-urinary antiseptic.*

GROUP OF HEXAMETHYLENAMINE.

HEXAMETHYLENAMINE, formerly known under the proprietary name of urotropine, together with its compounds, helmitol and citrarin, is **excreted** *by the kidneys, decomposed into ammonia and formaldehyde.* This excretion also takes place in

other parts of the body, as in the gall-bladder, etc. On account of the presence of the latter in the urine, these substances are among the most *powerful urinary antiseptics*. In cases of typhoid fever with many Eberth bacilli in the urine, it has been shown that urotropine causes a more rapid disappearance of these bacteria than would normally occur. In animals, large quantities of these substances may produce albuminuria and hæmaturia. Hexamethylenamine or its products, chinotropin, saliformin and hetralin, form soluble compounds with uric acid, but whether or not this combination helps the excretion of the latter, still remains to be decided.

A few "**GOUT REMEDIES**" may be conveniently mentioned now. When the theory was evolved that the cause of gout was the overproduction, precipitation and retention of uric acid, physicians administered alkalies with the idea of dissolving or keeping in solution the difficultly soluble uric acid and thus to facilitate its excretion. No remarkable results were obtained from the alkali metals and earths, so organic bases were tried. These form very soluble salts with uric acid and among them are **piperazine** and its compounds, including **sidonal, lycetol** and **lysidine.** More recently the question was attacked from another aspect. **Quinic acid,** a substance present in the bark of cinchona and many other trees is said to decrease the formation of uric acid and itself is transformed and excreted as hippuric acid. Different compounds of quinic acid with the same action are **urol, urocol, urosin,** and **sidonal.**

SUMMARY OF GROUP ACTION.—*Excretion by the kidneys with stimulation after small doses, and irritation of these organs with large quantities. Antiseptic action on the genito-urinary tract. With too great doses, gastro-intestinal irritation.*

THERAPEUTIC APPLICATION.—Preparations of **cubeb, copaiba** and **sandalwood** have been used so extensively in the treatment of *gonorrhœa* of the genito-urinary tract that they are almost regarded as specifics in this disease. Since the urine, after their ingestion, does not check the growth of the gonococci, it is probable that they do not produce their good effect by destroying

these bacteria, but by preventing the decomposition of the urine remaining in contact with the diseased membrane and so decreasing the irritation and the lowering of the vitality of the tissues which would afford a better field for the development of the disease. The best results are to be obtained in the earlier stages of this affection, but in the chronic form, and gleet, but little improvement is observed. These oils and their preparations are also indicated in *acute inflammation of the bladder and pelvis of the kidneys*. They increase the flow of urine through their irritant action upon the renal tissue, and may be used as *diuretics* when there is no acute inflammation or extensive degeneration of the kidneys. Their stimulant and disinfectant effect upon the bronchial mucous membranes recommends them in dry *bronchitis*.

Of late years the artificial bodies **hexamethylenamina** or **urotropine, helmitol** and **citrarin, chinotropin, saliformin** and **hetralin** have come in vogue as substitutes for the substances previously mentioned. They are more efficacious in *acute cystitis* and *pyelitis* because their antiseptic action is more marked; although, like the oils, they are of but little value in chronic inflammation of the urogenital tract. Their efficacy in acute gonorrhœal urethritis is warmly endorsed by many physicians.

Hexamethylenamine has been employed internally as an *antiseptic to the gall-bladder*, also in case of purulent ears, in colds in the nose with infections of sinuses and with inflammation of serous cavities, as in pleurisy, synovitis, etc.

All the members of the Hexamethylenamine division have been and are used for gout by some doctors, yet most authorities have observed very little good effect from any of them. It is not surprising, for we know very little about the cause of this trouble and uric acid seems to be more a product than a causative factor in the disease.

MATERIA MEDICA.

Cubeb and Copaiba Division.

Copaiba (U.S.P.,B.P.), Balsam of Copaiba, Copaiva, the oleoresin of Copaiba Langsdorffii and of other species of Copaibæ. **Dose:**—0.5–1.0 c.c. Br. (½–1 fl. dr.). Average (U.S.P.) 1 c.c.

Oleum Copaibæ (U.S.P.,B.P.), the oil freed from the resin by distillation. **Dose:**—0.5–1 c.c. (10–15 ♏). Average (U.S.P.) **0.5 c.c.**

Cubeba (U.S.P.), Cubebæ Fructus (B.P.), Cubebs, the unripe fruit of Piper Cubeba, containing the oil of cubeb and cubebin. **Dose:**—2–8 G. (30–120 grs.) in powder. Average (U.S.P.) **1 G.**

Oleoresina Cubebæ (U.S.P.). **Dose:**—0.5–1 c.c. (10–15 ♏). Average (U.S.P.) **0.5 G.**

Oleum Cubebæ (U.S.P.,B.P.). **Dose:**—0.5–1 c.c. (10–15 ♏). Average (U.S.P.) **0.5 c.c.**

Oleum Santali (U.S.P.,B.P.), Sandalwood oil, distilled from the wood of Santalum Album. **Dose:**—0.5–1 c.c. (10–15 ♏). Average (U.S.P.) **0.5 c.c.***

Buchu (U.S.P.,B.P.), leaves of Barosma Betulina. **Dose:**—2.0–4.0 G. Br. (½–1 ʒ). Average (U.S.P.) **2.0 G.**

Fluidextractum Buchu (U.S.P.). **Dose:**—2.0–4.0 c.c.

Uva Ursi (U.S.P.), leaves of Arctostaphylos Uva Ursi or Bearberry.

Fluidextractum Uva Ursi (U.S.P.). **Dose:**—5.0–15.0 c.c.

Hexamethylenamina Division.

Hexamethylenamina (U.S.P.), known under the trade names of urotropine, uritone, cystogen, cystamine, formin, aminoform, ammonioformaldehyde, composed of colorless crystal with bitter sweet taste, easily soluble in water. **Dose:**—Average (U.S.P.) **0.25 G.**

Helmitol and **Citrarin**, white crystalline compounds of hexamethylenamina and citric acid. **Dose**, same.

Liquor Formaldehydi (U.S.P.). Formaline, a 37 per cent. solution of formaldehyde gas in water. Used as a disinfectant of utensils, etc.

Chinotropin and **Chinoformin**, quinic acid compounds of hexamethylenamine. **Dose**, same.

Piperazina, crystals easily soluble in water. **Dose:**—1–2 G.*

GROUP OF VEGETABLE PURGATIVES.

The following is also a group of local irritants like the preceding ones. Many of its members when applied to the skin produce very severe irritation, as, for example, croton oil. In medicinal doses the various purgatives do not produce, when taken internally, severe irritation of the entire alimentary canal including mouth, œsophagus, stomach, small and large intestines, but they exhibit their effects more or less specifically on the lower portion of the gastro-intestinal tract where many of these are excreted even after subcutaneous administration.

Recent work has shown a well-marked selectiveness of different members of this group for certain parts of the gastro-intestinal

tract, whether they are introduced by mouth or intravenously. Thus, Magnus, by the *x*-ray method, has shown that senna has no action on the stomach and small intestines, while castor oil increases the peristalsis of the small intestine actively but not of the stomach. Castor oil caused purgation by decreasing the antiperistaltic activity of the large intestine, while senna acts as a distinct stimulant to peristalsis of the colon, besides, by special stimulation, when in the cecum, it causes reflex defecation. Padberg, a pupil of Magnus, investigated the mode of action of colocynth and found that it sometimes increases and sometimes decreases the emptying of the stomach. However, it always stimulates the peristalsis of the small intestine and inhibits the antiperistalsis of the large intestine. It causes defecation only by the rectal reflex and not by the cecal reflex, like senna.

This group comprises many substances of very different compositions extracted from the vegetable kingdom. Some of these are oils, as castor and croton oils, others are anthracene derivatives, as chrysophanic acid and emodin. Still others are glucosides as podophyllin and podophyllotoxin and finally others are acid anhydrides like elaterin.

These substances all have one property in common, that of *increasing the peristalsis of the intestine* by special local irritant action. They produce hyperæmia and it is probable that they increase both the movements and secretions of the intestinal tract. The **secretions** are only markedly increased after very large doses and assume the character of exudates, while the more fluid nature of the stools with small doses is due to the hastened **peristalsis** which does not allow of the reabsorption of the fluids. The increase in peristalsis is not only in the large intestines, but also in the small ones, and with the drugs, aloes and rhubarb, an increase in the movements of the stomach is also observed.

After copious doses of these purgatives, the evacuations are watery and the patient suffers from stomachache and cramps, probably due to the violent spasmodic contraction of the intestines, but the sensitiveness of the abdomen after too large quantities is due to actual inflammation.

They have much *less effect upon the stomach* than upon the intestines, because many require for their solution and preparation alkaline juices, as the bile and pancreatic secretions. Castor oil, for instance, has no action before it is changed to ricinoleic acid, which takes place much more readily in the small intestines than in the stomach.

Most purgatives, while producing a hyperæmia of the intestines, also produce a *congestion of the neighboring generative organs*. In this way they may increase hemorrhage from the uterus at the times of menstrual periods, or they may set up contractions of this organ and bring about abortion during pregnancy.

Some of these cathartics, as podophyllin, podophyllotoxin, colocynthin and croton oil act as purgatives when given subcutaneously. It is probable that their action is due at least in part to **excretion** by the intestinal mucous membranes. They produce severe irritation at the place of application, and also of the kidneys, and are, therefore, impracticable when administered subcutaneously.

Depending upon the dose and susceptibility of the patient, most purgatives act in from 6 to 10 hours. Aloes may not produce its effect before fifteen hours. Croton oil may act in two hours.

In habitual constipation, which is so frequent with the sedentary habits of modern life, it is very common for physicians to prescribe and patients to use on their own authority, various drugs of this group for periods of months and years, but almost always with a growing decrease in the effects produced. Many of these patients show on examination, a tender, thickened colon which is probably the result of the long chronic irritation that might have been avoided if, instead of irritants, exercise and regulation of the diet had been prescribed for the constipation.

Although the pharmacological action of the purgatives or that part of it which we know at the present, does not present sharp features of distinction, yet for convenience, they are divided into four groups based chiefly on their chemical composition.

CASTOR OIL DIVISION.

This subdivision includes two oils, Castor and Croton oils, which although quite different in strength act more or less in the same manner, i. e., after decomposition into fatty acids.

CASTOR OIL or **RICINOL** is very bland and unirritating and when pure, causes no stimulation of the skin, mouth, throat or stomach, but on reaching the small intestines it becomes saponified and ricinoleic acid and ricinoleates are formed which have a marked **irritant action** and by this means increase the intestinal peristalsis. If ricinoleic acid or ricinoleates are applied to the skin or given internally, redness of the epidermis, a burning acid taste in the throat, nausea, and vomiting occur. As a rule, no constitutional disturbance follows the ingestion of even large doses of castor oil and not even severe gastro-intestinal inflammation. It seldom produces much griping or pain.

This action, however, only applies to the expressed oil, for the castor beans themselves are very toxic; one has produced fatal poisoning, which consists of exceedingly severe gastro-enteritis with excruciating pains in the abdomen, nausea, vomiting, cyanosis, failure of the heart and respiration, and death in collapse. This very toxic action is due to the presence of a toxalbumin called **RICIN,** but as it is not soluble in oils it remains behind while expressing the castor beans.

CROTON OIL is a much more powerful purgative than the preceding. If more than a very small dose is given, it produces vomiting and purging (which may be bloody), intense cramps, tenderness of the abdomen and general collapse. With small doses, as a fraction of one drop, it causes only profuse, watery purgation.

Its action is due to the decomposition of croton oil into tigliic acid, a change which takes place very readily in the small intestines. Ordinary commercial croton oil, as a rule, contains considerable of this acid preformed, so that it is in contrast to castor oil, very irritating. If injected into the **skin** it produces violent inflammation with pustulation. It causes a burning sensation along the throat, œsophagus and stomach, and often induces

vomiting. The chemically pure croton oil containing no free tigliic acid is absolutely as bland and unirritating to the skin as olive oil yet it produces as much irritation of the bowels and purging as the commercial because it is decomposed there into the acid.

ALOIN AND RHUBARB DIVISION.

A number of crude drugs, as **RHUBARB, ALOES, SENNA, CASCARA,** and **FRANGULA,** contain the same or some very closely allied chemical substances which are *anthracene derivatives.* Among them are *emodin, chrysophanic acid, cathartin, frangulin* and *aloin* which have purgative action, but strangely enough, not so powerful as the crude drugs.

The amount of purgation induced by all these substances depends upon the quantity and form of administration and also upon the class of animal receiving them.

Emodin, cathartin, frangulin and the amorphous **aloin** produce purgation when isolated from the mother substance. **Chrysophanic** acid when given pure does not cause purgation because it is too rapidly absorbed. It is possible that in crude drugs mixed with colloids, it is less rapidly absorbed and much more active. This acid is again excreted by the urine, to which it imparts a yellow color often seen after taking rhubarb and senna. The milk of nursing women may also have a yellow color and purge babies, after taking these drugs.

Aloin, frangulin and **cathartin** are *purgatives when injected subcutaneously* and probably produce this effect through **excretion** *by the bowels* which has been proved for aloin. The latter does not irritate the kidneys in man, dogs and cats, but produces very destructive processes in rabbits. *Aloin produces marked peristalsis of the stomach.*

PHENOLPHTHALEIN DIVISION.

This includes phenolphthalein and its various derivatives and allies, but the title substance is the chief one used in medicine at present.

Phenolphthalein, its derivatives and allies act as purgatives in man, but much more slowly than the crude vegetable purgative drugs, sometimes only in twenty or twenty-four hours. Phenolphthalein and its tetra-chlor derivative exert a laxative or purgative action also when given subcutaneously and intravenously. When a solution of the tetra-chlor derivative of phenolphthalein (0.4 G.) in oil is injected under the skin of dogs and human beings, a laxative action is induced which lasts from four to six days.

These phthaleins are non-irritant when applied to mucous membranes or wounds or injected subcutaneously in oily solution. Their sodium and potassium salts, however, are very irritant.

When phenolphthalein is injected subcutaneously it escapes both by the bile and urine, but the tetra-chlor compound only leaves by the bile. After internal administration, none of the tetra-chlor derivative leaves by any other channel than the intestine. An interesting proof of the selectiveness of these compounds on certain parts of the intestines is that only the cells of the large intestine take up tetra-chlor phenolphthalein, while those of the small intestine take up none whatever. Phenolphthalein gives the urine a bright red color when the latter is alkaline.

Purgatine, trioxyanthrachinon, causes purgation in man, but when given to rabbits produces a yellowish, then a brownish-red port-wine color in the urine and without causing any purgation the animals die with extensive destruction of the kidney and loss of weight just as with aloin. In dogs, although the urine is colored red, no serious symptoms appear even after taking the drug for a period of months.

ELATERIN AND PODOPHYLLIN DIVISION.

The acid anhydrides and glucosides Elaterin, Jalapin, Convolvulin, Scammonin, Colocynthin, Podophyllotoxin and Picropodophyllotoxin form a division of very active cathartics which give rise to watery evacuations. **Elaterin, jalapin** and **convolvulin** require the presence of bile to dissolve them before they act, just as does aloes; but bile also helps the action of all the

other purgatives. **Podophyllotoxin, picropodophyllin** and **colocynthin** cause purgation when injected subcutaneously. This is due to a partial **excretion** *by the intestines*. They cause violent irritation at the place of injection and are very apt to bring about severe inflammation of the kidneys due to excretion of part of these substances by the latter organs. All the members of this division are much more irritant than those of the rhubarb group and in sufficient doses give rise to vomiting and diarrhœa, often of a bloody character, with reddening and ecchymoses of the intestinal mucosa. The irritation may be so severe as to produce collapse. With podophyllotoxin even a pseudomembrane formation has been observed.

SUMMARY OF GROUP ACTION.—*Special stimulation and irritation of the bowels leading to purgation. With large doses actual inflammation of gastrointestinal tract. By subcutaneous administration catharsis, also violent irritation at place of application and of kidneys.*

THERAPEUTIC APPLICATION.—Almost all the members of this group may be used in small doses to produce mild evacuations of the bowels and thus relieve *constipation*, or in large doses to cause severe purgation. For convenience the milder ones, such as **castor oil, senna, aloes, rhubarb** and **cascara** are used as *laxatives* and *mild purgatives*, while **croton oil, jalap, colocynth, podophyllum** and **camboge** are used as *drastics*, i. e., for severe purgative action.

Croton oil is used almost exclusively in unconscious patients, especially those suffering from *apoplexy*. Here it is supposed to do good by lowering the blood pressure and thus aiding the arrest of the hemorrhage. This it may do both by producing a dilatation of the splanchnic blood vessels and by decreasing the bulk of blood through watery evacuations.

The use of purgatives is indicated in all cases when the intestine is to be emptied, as after poisoning from drugs and from food products, or when there is infection of the intestines, as in *typhoid fever*, or *autointoxication* due to fermentation or putrefactive changes in the intestinal contents.

They should not be used when there is severe inflammation of the intestines, and only with caution during pregnancy. As a rule the active principles do not act so well as the crude drugs, probably because the colloidal substances in the latter prevent rapid absorption and decomposition, thus keeping them longer in contact with the mucous membrane.

MATERIA MEDICA.

Simple Purgative Series.

Oleum Ricini (U.S.P.,B.P.), castor oil, a yellowish, viscid fixed oil expressed from the seeds of Ricinus Communis. It has a very disagreeable odor and taste. The seeds contain besides this oil, the toxalbumin, ricin, which, however, is not extracted by expression of the oil. **Dose:**—5.0–50.0 c.c. Br. (1–8 fl.ʒ). Average (U.S.P.) **16.0 c.c.**

Senna (U.S.P.), Senna Alexandrina (B.P.), the leaflets of Cassia Augustifolia and Acutifolia trees growing respectively in India and Africa. It contains the glucoside emodine and the glucosidal acids, cathartic acid and chrysophanic acid.

Infusum Sennæ Compositum (U.S.P.) (black draught) contains senna, manna, magnesium sulphate and fennel. **Dose:**—25.0–50.0.

Infusum Sennæ (B.P.). **Dose:**—½–1 fl.ʒ.

Pulvis Glycyrrhizæ Compositus (U.S.P.) (compound licorice powders) contains senna, sulphur, fennel, sugar and licorice. **Dose:**—2.0–8.0. Average (U.S.P.) **4.0 G.**

Aloe Socotrina (U.S.P.), inspissated juice from Aloe Perriji, a tree growing in Africa and Isle of Socotra. Aloe Barbadensis (B.P.), inspissated juice from Aloe Vera. They are formed of brown resinous masses and contain the neutral principle aloin, emodin and a resin.

Extractum Aloes (U.S.P.,B.P.). **Dose:**—0.03–0.2 G. Br. (1–4 grains). Average (U.S.P.) **0.125 G.**

Aloe Purificata (U.S.P.). **Dose:**—0.03–0.5 G. Average (U.S.P.) **0.25 G.**

Tinctura Aloes. Dose:—1.0–4.0. Br. (½–1ʒ). Average (U.S.P.) **2.0 c.c.**

Pilula Aloes. Dose:—1–4 pills. Br. (4–8 grains).

Aloinum. Dose:—0.05–0.2. Br. (½–2 grains). Average (U.S.P.) **0.065 G.**

Rheum (U.S.P.) or rhubarb, the roots of Rheum Officinale, and Rhei Radix (B.P.), root of Rheum Palmatum containing chrysophanic acid, emodin, cathartin and a resin.

Pilulæ Rhei Compositæ (U.S.P., B.P.). **Dose:**—1–5 pills.

Tinctura Rhei (U.S.P., B.P.). **Dose:**—4–16 c.c. Br. (1–4 ʒ). Average (U.S.P.) **2.0 c.c.**

Tincturæ Rhei Composita (B.P.). **Dose:**—½–1 ʒ.

Frangula (U.S.P.), or Buckthorn, the bark of Rhamnus Frangula, a tree growing in Asia and Europe. It contains emodin and frangulin.

Fluidextractum Frangulæ (U.S.P.). **Dose:**—2.0–8.0. Average (U.S.P.) **1.0 c.c.**

Rhamnus Purshiana (U.S.P.), or Cascara Sagrada (B.P.), the bark of Rhamnus Purshiana, a tree growing in California and Spanish North America. It contains emodin and cascarin.

Fluidextractum Rhamni Purshianæ (U.S.P.). **Dose:**—2.0–8.0 c.c. Average (U.S.P.) **1.0 c.c.**

Extractum Cascaræ Sagradæ Liquidum (B.P.). **Dose:**—⅓–1 fl. ʒ.

Phenolphthalein, white crystalline body difficultly soluble in H_2O, turning red in the presence of alkalies. **Dose:**—0.1–0.2 G.

Exodin is a mixture of anthraquinone derivatives. **Dose:**—0.5–1.0 G.

Drastic Series.

Scammonium (U.S.P.), Scammoniæ Radix (B.P.), resinous exudate from the roots of Convolvulus Scammonia, an herb growing in Asia and Greece. It contains the glucoside Jalapine.

Resina Scammoniæ (U.S.P.). **Dose:**—0.05–0.5 G. Average (U.S.P.) **0.2 G.**

Scammoniæ Resina (B.P.). **Dose:**—3–8 grains.

Jalapa (U.S.P., B.P.), the tuberous roots of Ipomœa Jalapa, a plant growing in Mexico and India and containing the glucosides jalapin and convolvulin.

Extractum Jalapæ (B.P.). **Dose:**—0.1–0.5 G. Br. (2–5 grains).

Resina Jalapæ (U.S.P.,B.P.). **Dose:**—0.5–0.3. Br. (2–5 grains). Average (U.S.P.) **0.125 G.**

Pulvis Jalapæ Compositus (U.S.P., B.P.), containing jalap and potassium bitartrate. **Dose:**—1.0–4.0. Br. (15–60 grains). Average (U.S.P.) **2.0 G.**

Oleum Tiglii (U.S.P.), Oleum Crotonii (B.P.), a fixed oil expressed from the seeds of Croton Tiglium, a tree growing in India and the Philippines. The oil usually contains free tigliic or croton oleic acid. **Dose:**—0.005–0.10 c.c. Br. (⅓–1 ♏). Average (U.S.P.) **0.05 c.c.**

Colocynthis (U.S.P.), Colocynthidis Pulpa (B.P.), fruit of Citrullus Colocynthis, which grows in Asia and Africa and contains Colocynthin.

Extractum Colocynthidis Compositum (U.S.P.,B.P.). **Dose:**—0.03–0.1 G. Br. (3.15 grains). Average (U.S.P.) **0.5 G.**

Elaterinum (U.S.P., B.P.), a neutral principle obtained from the juice of the fruit of Ecballium Elaterium or Squirting Cucumber. It is composed of white crystals with an acrid bitter taste. **Dose:**—0.002–0.005 G. Br. $\frac{1}{16}$–$\frac{1}{10}$ grain). Average (U.S.P.) **0.005 G.**

Trituratio Elaterini (U.S.P.). **Dose:**—0.03–0.05. Average (U.S.P.) **0.03 G.**

Podophyllum (U.S.P.), Podophylli Rhizoma (B.P.), rhizome and roots of Podophyllum Peltatum, which grows in America. It contains the isomeric glucosides podophyllotoxin and picropodophyllin.

Resina Podophylli (U.S.P.), Podophylli Resina (B.P.). **Dose:**—0.05–0.2 G. Br. (1–3 grains). Average (U.S.P.) **0.05** laxative; **0.015** purgative.

Podophyllotoxin. Dose:—0.005–0.06.

Euonymus (U.S.P.), Euonymi Cortex (B.P.), the dried root bark of Euonymus Atropurpureus or Spindle tree, contains the glucoside Euonymin which is both a purgative and heart poison and also the glucoside atropurpurin.

Extractum Euonymi (U.S.P.). **Dose:**—0.05–0.3 G. Average (U.S.P.) 0.125 G.

Extractum Euonymi Siccum (B.P.). **Dose:**—1–2 grains.

Cambogia (U.S.P., B.P.), gum resin from Garcinia Hanburii, which grows in Siam, Anam, Cambogia and Cochinchina. It contains the resinous acid, cambogic acid.

Pilulæ Catharticæ Compositæ (U.S.P.) contain besides camboge, calomel, colocynth and jalap. **Dose:**—1–3 pills.

Pilulæ Cambogia Composita (B.P.). **Dose:**—4–8 grains.

GROUP OF BITTERS.

Bitter medicines, such as quassia, have been used for a long time as remedies in the treatment of digestive disturbances and in a certain number of cases the appetite returns and patients improve.

A large number of bodies isolated from plants which have the common characteristics of possessing a bitter taste, form this group. Among these are alkaloids, glucosides, acids, and neutral bodies, all of which have little or no general action in the doses used in medicine. Such bitter alkaloids as strychnine and quinine, which have a powerful constitutional action, are excluded. The substances belonging to this division are not devoid of constitutional action, but on the contrary, such bodies as Berberine, Canadine, Lupulinic Acid, etc., may produce very severe poisonous effects when given in excessive doses intravenously to animals; but when given in ordinary doses internally to man, they cause none but the local effect on the gastro-intestinal tract.

SIMPLE BITTERS *produce in man, as a rule, increase in the appetite, and secondarily an augmentation in the gastric secretion which is due in main part to reflex stimulation through the gustatory nerves, on account of the bitter taste.*

The increase in **gastric secretion** is best seen when a meal containing meat is given soon after the bitters, and may amount to 25 per cent. above the normal. Being more or less irritant, they cause a hyperæmia of the mucous membrane of the gastro-intestinal tract which leads to an increase in the **absorption** of food stuff. They also augment the **movements of the stomach**

and small intestine. After very large doses, or in subjects with hyperacidity, they cause a burning along the œsophagus and stomach, sometimes even nausea and vomiting. The bitters increase the leucocytes in the blood and also for this reason may increase the absorption and transportation of nutriments from the stomach and intestines into the various tissues.

There are a certain number of crude drugs, as bitter orange, cardamom, cinnamon and ginger, which are called **AROMATIC BITTERS** and they contain besides a bitter principle, a volatile oil which reinforces their action and gives them a greater tendency to irritate the mucous membranes.

SUMMARY OF GROUP ACTION.—*Through their bitter taste, stimulants to appetite and through their local irritant action stimulants to the digestive secretions of the alimentary canal. Too large doses produce marked irritation with nausea, vomiting and diarrhœa.*

THERAPEUTIC APPLICATION.—The **bitters** are used almost exclusively in the form of crude preparations to *increase the appetite* and *improve the digestion* in cases of malnutrition from almost any cause, as *consumption, cancer, anæmia, neurasthenia* and *dyspepsia.* Their use is not attended with good results in cases with hyperacidity and ulcer, because they may further increase the hydrochloric acid and sensitiveness of the stomach.

In former times, one of these bitters, **condurango,** was used as a specific against cancer. The results obtained were not sufficiently good to warrant the continuance of this remedy. Undoubtedly temporary improvement obtained in cases of gastric carcinoma was due to the bitter action of this drug in increasing appetite and facilitating digestion.

MATERIA MEDICA.

Simple Bitters.

Quassia (U.S.P.), Quassia Lignum (B.P.), wood of Picrasma Excelsa, a tree growing in Jamaica. It contains quassin, a neutral body, and is said to produce headaches, nausea and vomiting in too large doses.

Fluidextractum Quassiæ (U.S.P.). **Dose:**—1.0–2.0 c.c. Average (U.S.P.), **0.5 c.c.**

Tinctura Quassiæ (U.S.P., B.P.). **Dose:**—2.0–4.0 c.c. Br. (15–60 ♏). Average (U.S.P.) 2 c.c.

Condurango, Gonolobus bark, vine of Ecuador, contains 2 alkaloids, a glucoside and a resin. The glucoside injected in dogs produces ataxia and convulsions. **Dose:**—1.0–2.0 G.

Calamus (U.S.P.) contains the glucoside acorine and the alkaloid calamine. **Dose:**—Average (U.S.P.), 1.0 G.

Fluidextractum Calami (U.S.P.). **Dose:**—1.0–4.0 c.c. Average (U.S.P.), **1.0 c.c.**

Cimicifuga (Racemosa), black snakeroot, native of North America. Contains bitter resin and tannic acid.

Fluidextractum Cimicifugæ. **Dose:**—1.0–4.0 G.

Cusparіæ Cortex (B.P.), Angostura bark from tropical South America contains cusparine and other alkaloids. **Dose:**—0.5 to 2.0 G.

Infusum Cusparіæ (B.P.). **Dose:**—1–2 fl. ʒ.

Calumba (U.S.P.), Calumbæ Radix (B.P.), the roots of Jateorrhiza Palmata, which grows in Africa and East Indies and contains the neutral columbin, the alkaloid berberine and columbic acid.

Tinctura Calumbæ. **Dose:**—4–15 c.c. Br. (1–4 fl. ʒ). Average (U.S.P.), **4.0 c.c.**

Gentiana (U.S.P.), Gentiana Radix (B.P.), root of Gentiana Lutea. It contains the glucoside gentiopicrin and the neutral body gentisin.

Extractum Gentianæ (U.S.P., B.P.). **Dose:**—0.1 to 0.5 G. Br. (2–10 grains). Average (U.S.P.), **0.25 G.**

Tinctura Gentianæ Composita (U.S.P., B.P.). **Dose:**—1.0–15.0 c.c. Br. (¼–4 fl. ʒ). Average (U.S.P.), **4.0 c.c.**

Cetraria (Icelandica) contains lichenin and cetraric acid.

Decoctum Cetrariæ, 30–100 c.c.

Chirata (B.P.), from Swertia Chirata, grows in India and contains the glucoside chiratin and ophelic acid.

Tinctura Chiratæ (B.P.). **Dose:**—2.0–8.0 c.c. Br. (1–2 fl. ʒ).

Humulus (U.S.P.), **Lupulus** (B.P.), hops, grows in America and Europe. It contains lupulin and lupulinic acid and a resin. Lupulin when injected into animals produces first stimulation then depression of the medulla. **Dose:**—Average (U.S.P.), **2.0 G.**

Tinctura Lupulini (B.P.). **Dose:**—½–1 fl. ʒ.

Coto, bark of tree growing in Peru. It contains cotoin.

Fluidextractum Coto. **Dose:**—0.3–2.0 c.c.

Cornus (Florida), dogwood, grows in North America and contains cornin.

Extractum Cornі, 1.0–2.0 c.c.

Serpentaria (U.S.P.), Serpentaria Rhizoma (B.P.), from Aristolochia, Virginia snake-root, contains the alkaloid aristolochine.

Fluidextractum Serpentaria (U.S.P.). **Dose:**—1.0–2.0 c.c. Average (U.S.P.), **1.0 c.c.**

Tinctura Serpentaria (U.S.P., B.P.). **Dose:**—2.0–8.0 c.c. Br. (½–1 fl. ʒ). Average (U.S.P.), 4.0 c.c.

Taraxacum (U.S.P.), Taraxacum Radix, root of dandelion, or Taraxacum Officinale, contains taraxacin and taraxacein.

Fluidextractum Taraxaci (U.S.P.). **Dose:**—1.0–10.0 c.c. Average (U.S.P.), 8.0 c.c.

Succus Taraxaci (B.P.). **Dose:**—1–2 fl. ʒ.

Orexine Hydrochlorate, artificial base, composed of colorless crystals, soluble in 15 parts of water. It has a bitter sharp taste. When injected into animals it produces tremors, convulsions, dyspnœa and methæmoglobinæmia when mixed with blood, but in man it produces no symptoms but those referable to the bitter action. **Dose:**—0.1 to 0.3 G.

VEGETABLE ASTRINGENTS.

Astringents *are substances which make an insoluble and contractile compound with proteid and in so doing, upon abraded surfaces or mucous membranes, check the secretions, arrest hemorrhage and decrease congestion.* In great concentration, most astringents are irritant and some even caustic as they attack the life of the living cells.

Astringents are of two kinds, vegetable and metallic, but in this place we will concern ourselves only with the former and leave the latter to be described under the groups of metals.

GROUP OF TANNIC ACID.

In the root, wood and bark of many trees, we find some variety of tannin or tannic acid. The extracts of those of oak, sumach and witch hazel have been used for many years to check hemorrhage, to decrease secretions and to control inflammations of mucous membranes.

This application is based on the property which **TANNIC ACID** possesses of precipitating proteids and albuminoid substances into a white, tough, contractile compound: it is with tannic acid that hides are transformed to leather. When it is applied over wounds or mucous membranes, the layer of the albuminous compound, by contraction, squeezes the vessels and glands underneath. By this pressure and the direct chemical combination between the proteid of the gland and the tannic acid, the secretions are stopped.

In very diluted solutions, this acid constricts **blood vessels** and also stops the movements of the leucocytes and their diapedesis through their vessel walls. In this way **inflammatory processes** may be controlled. Very strong solutions are irritant

and may cause the reverse, i. e., dilatation of blood vessels and inflammatory reactions.

Superficial **hemorrhages** are arrested by the narrowing of the vessels due to the squeezing of the contractile membrane over them and also by a thrombus formation in their lumen, due to the precipitation of the proteids of the blood by the tannic acid.

When it is taken internally, there is a puckery feeling in the mouth, throat and tongue. The latter also loses some of the perception of taste. If the solution is a diluted one, as a rule, no further symptoms except constipation are observed. These are all due to the precipitation of the albumin in the superficial layers of the mucous membrane. If, on the other hand, much of a concentrated solution is imbibed, there occur nausea, vomiting, and frequently diarrhœa which result from the irritant action of large quantities; therefore the **symptoms** after the ingestion of too large doses of tannic acid are those of gastro-enteritis.

The proteid compounds of tannic acid are dissolved by gastric juice, acids and alkalies. After having acted in the stomach they may again produce an astringent effect on the bowels. The astringent action of tannic acid stops, however, when, as ultimately occurs in warm-blooded animals, the latter is **transformed** into gallic acid and is absorbed mainly as such. It is all **oxidized** in the body, except about one per cent., which reappears in the urine and feces in the form of both sodium tannate and gallic acid, but chiefly as the latter. Both these substances do not precipitate proteids and have in consequence no astringent effect, so that the use of these or of tannic acid internally for this action on remote organs, as kidneys and lungs, cannot be attended with good results. The intravenous injection of tannic acid is not practicable because it causes embolism and death by precipitating the proteids of the blood.

The urine, on standing, sometimes develops pyrogallol from the decomposition of the gallic acid.

The **crude preparations** of this group, as the extracts of hamamelis, oak, catechu, etc., do not affect the stomach as much as pure tannic acid, because it requires a certain length of

time for the tannin to be extracted from the colloids in these; so that they have always been chosen instead of the pure preparations when an astringent effect on the bowels was desired.

Lately, however, there were introduced newer artificial compounds of tannic acid with albumen and different substances which prevent the decomposition and action on the stomach, but which are readily dissolved and decomposed by the pancreatic juice and exert marked astringent action on the intestines. Among these bodies are **Tannalbin, Tannigen, Tannocoll** and **Honthin.**

SUMMARY OF GROUP ACTION.—*Formation of insoluble compounds with proteids over mucous membranes and abraded surfaces, causing a decrease of secretions, congestion and of hemorrhage with small amounts, but marked congestion and inflammation with large quantities.*

THERAPEUTIC APPLICATION.—A solution of **tannic acid** is used externally over *bleeding wounds* in the skin or external mucous membranes, as nose, mouth and pharynx. It is also employed in the form of injections in the treatment of inflammatory conditions of the vagina, urethra and large intestines, as *gonorrhœal vaginitis*, *urethritis* and *ulcerative colitis*.

Tannic acid is not used uncombined internally because it produces too much action upon the stomach. In former times, in its place the crude extracts containing tannin were employed because they contained colloidal material which prevented it from acting so readily upon the gastric mucosa.

Lately the undesirable effect upon the stomach has been in good part obviated by the use of artificial preparations, **tannigen, tannalbin, tannopin** and **honthin,** which are not readily or not at all dissolved in the stomach, but are decomposed by the alkaline secretions of the intestine where they can assert their astringent action. They are valuable in diarrhœa from catarrhal or ulcerative conditions.

MATERIA MEDICA.

Acidum Tannicum (U.S.P., B.P.), tannic acid, tannin or gallotannic acid, an organic acid extracted from nutgall. It is a yellowish, amorphous,

scaly powder with slight odor and astringent taste, soluble in 1 part of H_2O, 0.6 part of alcohol and 1 part of glycerine. **Dose:**—0.1–0.5. Br. (2–10 grains). Average (U.S.P.), **0.5 G.**

Collodium Stypticum contains 20 per cent. tannic acid.

Trochisci Acidi Tannici (U.S.P.) contains 0.06 tannic acid. Dose:—1–3 troches.

Unguentum Acidi Tannici (U.S.P.) contains 20 per cent. tannic acid.

Glyceritum Acidi Tannici (U.S.P.), Glycerinum Acidi Tannici (B.P.), contains 20 per cent. tannic acid.

Acidum Gallicum (U.S.P., B.P.), pale yellow needles obtained from nutgall, soluble in 100 parts of water, 5 parts of alcohol, and 12 parts of glycerine. **Dose:**—0.3–1.0. Br. (5–15 grains). Average (U.S.P.), **1.0 G.**

Synthetic Tannic Acid Compounds.

Tannigen, acetic ester of tannic acid, tasteless, odorless powder, almost insoluble in H_2O, insoluble in gastric juice, but dissolved by alkalies and intestinal juices. **Dose:**—0.5–1.0 G.

Tannalbin, albuminous compound of tannic acid, light brown, odorless, tasteless powder, insoluble in gastric juice and water, but soluble in alkaline intestinal juices. **Dose:**—1.0–4.0 G.

Tannopin, compound of urotropine and tannic acid, brown, tasteless, odorless powder, insoluble in H_2O, weak acids and alcohol, but easily soluble in alkalies. **Dose:**—0.5–1.0 G.

Honthin, keratinized compound of tannic acid, same general properties as the above. **Dose:**—1.0–4.0 G.

Tannocol, compound of gelatine and tannic acid. Same general properties as the above. **Dose:**—1.0–4.0 G.

Tannoform, compound of formaldehyde and tannic acid. Same general properties as the above. **Dose:**—1.0–4.0 G.

Crude Preparations Containing Tannic Acid.

Galla (U.S.P., B.P.) (Nutgall), excrescence on Quercus Lusitanica caused by the punctures and deposited eggs of the insect Cynips Gallæ Tinctoriæ, smooth, hard, olive green body with a central cavity. It contains about 60 to 70 per cent. tannic and 2 to 3 per cent. gallic acid.

Tincturæ Gallæ (U.S.P.) contains 20 per cent. nutgall. **Dose:**—2.0–8.0 c.c. Average (U.S.P.), **4.0 c.c.**

Unguentum Gallæ (U.S.P., B.P.) contains 20 per cent. nutgall.

Quercus Alba (U.S.P.), the bark of Quercus Alba or white oak, contains quercitannic acid and quercin.

Fluidextractum Querci (U.S.P.). Dose:—1.0–4.0 c.c. Average (U.S.P.), 1.0 c.c.

Catechu (B.P.), an extract from the leaves of Acacia Catechu, contains catechu-tannic acid and catechuic acid.

Tinctura Catechu (B.P.). Dose:—½–1 fl. ʒ.

Krameria (U.S.P.), Krameriæ Radix (B.P.), the root of Krameria Triandra or rhatany, a plant growing in Peru and Bolivia, contains kramero-tannic acid.

Tinctura Krameriæ (U.S.P., B.P.). Dose:—1.0–10.0 c.c. Br. (½–2 fl. ʒ). Average (U.S.P.), 4.0 c.c.

Kino (U.S.P., B.P.), inspissated juice of Pterocarpus Marsupium which grows in the East Indies. It contains kino-tannic acid and kinoin, a neutral body.

Tinctura Kino (U.S.P., B.P.). Dose:—1.0–10.0 c.c. Br. (½–2 fl. ʒ). Average (U.S.P.), 4.0 c.c.

Hamamelidis cortex (U.S.P.), Hamamelidis Folia (B.P.), witch-hazel, leaves of Hamamelis Virginiana, which grows in North America and contains about 8 per cent. tannic acid.

Fluidextractum Hamamelidis Foliorum (U.S.P.). Dose:—2.0–8.0 c.c. Average (U.S.P.), **2.0 c.c.**

Extractum Hamamelidis Liquidum (B.P.). Dose:—5–15 ♏.

Hæmatoxylon (U.S.P.), Hæmatoxylon Lignum (B.P.) logwood, wood of Hæmatoxylon Campechianum, growing in Central America and West Indies. It contains tannic acid and 12 per cent. hæmatoxylin.

Extractum Hæmatoxyli (U.S.P.). Dose:—0.3–1.0 G. Average (U.S.P.). 1.0 G.

Decoctum Hæmatoxyli (B.P.). Dose:—½–1 fl. ʒ.

Rubus (U.S.P.), blackberry, the bark of the root Rubus Villosus Canadensis and Trivialis, growing in North America. It contains about 12 per cent. tannic acid and a bitter principle villosin.

Fluidextractum Rubi (U.S.P.). Dose:—2.0–8.0 c.c. Average (U.S.P.), **1.0 c.c.**

Rhus Glabra (U.S.P.), sumach, the fruit of Rhus Glabra growing in North America and containing 5 to 25 per cent. tannic acid.

Fluidextractum Rhois Glabræ (U.S.P.). Dose:—1.0–4.0 c.c. Average (U.S.P.), **1.0 c.c.**

WORM REMEDIES.

Although many substances which have been and are used to free the body of intestinal worms are not described in this section, yet we characterize the following two groups as those of anthelmintics or of worm remedies: they include the typical ones which are employed for no other purpose in medicine. Chloroform, salt, turpentine, oil of tansy, quassia and thymol are all used as anthelmintics, but they have other qualities and a typical action which place them in other divisions. On the other hand, **male fern, pomegranate** and **santonica** contain active principles whose action is not typical of any other group, and their exclusive use in therapeutics is as worm remedies.

The members of these groups are used both against the *round and tape worms*. The action of the drugs depends, in some cases, on a specific poisonous action towards the parasites, as with pelletierine, which destroys tape worm in a watery solution of 1 to 10,000. With others, such as male fern, the results are due

to the fact that the active principle is absorbed with great difficulty by the gastro-intestinal tract, much more slowly absorbed than by the worm, the latter, therefore, becoming destroyed long before poisonous symptoms arise in the afflicted individual.

When the worm remedies are given to a human being, occasionally it happens that the conditions are more than usually favorable for absorption, either they have been administered with a solvent drug or retained too long in the bowels, then well-marked poisonous symptoms may develop. Oil helps the solution and absorption of many of the anthelmintics, therefore such symptoms are especially apt to occur when an oil has been given with or after a worm remedy.

These anthelmintics have more or less selective action for the kind of worm: e. g., pelletierine and filicic acid act far more energetically on tape worms than santonine, while the reverse is true for round worms.

Formerly anthelmintics were classified as vermifuges, i. e., those which drove the worm from the small into the large intestine, from which it was subsequently expelled, and vermicides, i. e., those which killed the parasite. Whether the worms are killed or only sickened depends greatly upon the dose used, and upon the condition of the intestines, such as the presence of food, which has a tendency to protect the parasite; therefore this classification is a little too arbitrary.

GROUP OF PELLETIERINE.

Pomegranate, the typical tape worm remedy, contains besides tannin a number of closely related alkaloids, the principal ones being pelletierine or punicine and isopelletierine. Preparations of the crude drug are strongly irritant because of the large amount of tannic acid which they contain.

The active principles of the plant are the alkaloids, one of these, **PELLETIERINE,** being able to kill **tape worms** in the strength of 1 to 10,000, while it does not affect round worms in much stronger solutions.

When administered to human beings in too large doses, pelle-

tierine, but more especially crude preparations of the mother substance, pomegranate, are liable to produce much irritation of the **gastro-intestinal tract,** evidenced by pain in the abdomen, nausea, vomiting and diarrhœa. Besides the intestinal irritation there also occur some symptoms referable to an action on the central nervous system, such as headache, dizziness, disturbances of cerebration and vision, irritability, tremors, cramps in the limbs and even convulsions.

In frogs, pelletierine decreases the power of relaxation of skeletal **muscles** similarly to veratrine. It increases the reflex irritability of the **cord** which may lead to convulsions, but with very large doses it paralyzes the motor nerve endings just as curare.

Warm-blooded animals are not deeply susceptible to pelletierine, in fact, rabbits require almost 0.3 G. per kilo of their body weight to produce fatal results. With large doses, they exhibit an increased reflex irritability due to stimulation of the **cord,** and incoordination of movements probably caused by an action upon the cerebellum. *Death results from paralysis of the centres in the* **medulla,** and is, therefore, preceded by decreased respiration and by a fall of blood pressure.

When extract of **ASPIDIUM** or male fern is administered to a human being suffering from tape worm, as a rule no other symptom is observed except the poisoned or the dead worm in the stool which follows. When, however, too large quantities are used or when castor oil or other substances which aid the absorption of the poison have been administered, there may occur a series of **poisonous symptoms,** partly referable to gastro-intestinal disturbances and partly to an effect upon the central nervous system. These consist of nausea, vomiting, pain in the abdomen and diarrhœa, dizziness, headache, roaring in the ears, dimness of vision, muscular twitching, convulsions, weak pulse, superficial respiration, cyanosis, stupor, unconsciousness and death. At autopsy the inflammation of the stomach and intestines is always well marked and occasionally jaundice has been observed, probably from the destruction of the red blood cor-

puscles. The temporary and permanent blindness which has occurred in a few cases was possibly the result of degeneration of the retina, because such changes can be produced in dogs by male fern.

Of the various substances present in male fern, including resins, oils, neutral and acid bodies, etc., the most poisonous, which has the same action as extracts of the plant, is **FILICIC ACID,** or filicin. This acid is more poisonous to Tænias and Anchylostoma Duodenale than to other varieties of worms. It is, as a rule, very difficultly absorbed by the gastro-intestinal tract, although a few fatal cases of poisoning in man are probably due to its passage into the circulation.

In warm-blooded animals, filicic acid depresses the **medulla** at the same time that it increases the reflex irritability of the **cord.** Marked tetanic convulsions like those produced by strychnine may be observed. The paralysis of the medulla causes a fall of blood pressure and a decrease in the respiratory capacity. The **heart** is also paralyzed by this drug, so that death is due to both failure of respiration and circulation.

There is severe *gastro-intestinal inflammation* just as after the crude drug. The urine of rabbits may show evidence of *irritation of the kidneys* and also glycuronic acid. In frogs, it causes a marked weakening of the strength of both skeletal and cardiac **muscles** and general paralysis of the central nervous system.

ASPIDIN, another constituent of male fern, does not produce poisoning in warm-blooded animals when taken internally or subcutaneously, but produces death by paralysis of the **respiratory centre** when injected intravenously. In frogs it causes much, the same symptoms as filicic acid, but is more apt to produce twitchings and convulsions; while **aspidinin** has the same action, **albaspidin** gives rise to general paralysis like filicic acid.

Cusso, the Abyssinian anthelmintic, contains as an active principle **KOSSOTOXIN.** This drug has a bitter and disagreeable taste which is apt to cause nausea. The **symptoms of poisoning** in man, which are rarely observed, resemble closely those seen after an overdose of male fern, and consist of *gastro-*

intestinal irritation with abdominal pain, vomiting and defecation, and of *depression of the central nervous system* with weak, hurried respirations and collapse.

In frogs kossotoxin paralyzes the **motor nerve endings,** the skeletal and heart **muscles.** It produces convulsions after intravenous injection in rabbits. As it depresses the medulla, death is the result of respiratory arrest.

KAMALA is used in the Philippines and India as an anthelmintic. It is said to be less powerful than those previously mentioned. It produces considerable gastro-intestinal irritation resulting occasionally in vomiting, but more often in evacuation of the bowels.

PEPO or pumpkin seeds are employed in the United States for the removal of tape worm, but even in large doses they produce no pharmacological action upon animals.

GROUP OF SANTONIN.

SANTONIN is the remedy par excellence for **round worms,** which it poisons but does not kill. When these are exposed to solutions of santonin, they make lively convulsive movements, but do not die. It is possible that santonin may be so transformed by digestive juices as to be more active within the body, yet it is sufficient to assume that the worms made ill in the small, take refuge in the large intestine, where, because of their disability, they are easily expelled by purgatives. Frequently they leave the body in a state of active movements.

Although santonin is almost insoluble in water, it is to some extent dissolved by the juices of the alimentary canal and is partly absorbed, so that even after small doses there is seen in man disturbances of **vision,** and all objects look violet, then yellow. It is interesting to note that santonin is a derivative of naphthalene, which also produces disturbances of vision.

Large doses cause the following **symptoms:** nausea and vomiting, diarrhœa, headache, hallucinations, dizziness, tremor, convulsions, involuntary urination and defecation, albuminuria and

hæmaturia, unconsciousness and death from failure of respiration. It is believed that the convulsions are due to stimulation of the middle brain and later of the **medulla.** Extremely large doses also stimulate the cord. The respiratory and vasomotor centres are only depressed late in the poisoning. Santonin is **excreted** partly by the urine and feces in the form of santogenin, which colors these secretions a deep saffron color.

SPIGELIA, another round worm remedy, rarely produces the following poisonous **symptoms:** flushes and dryness of the skin, hallucinations, somnolence and disturbances of vision. When administered subcutaneously to the lower animals, there occur vomiting, incoordinate gait, labored breathing, coma and death, which is due to *respiratory failure*, often preceded by convulsive attacks.

SUMMARY OF GROUP ACTION.—*Either special toxic properties towards intestinal parasites or difficult absorption by the gastro-intestinal tract permits of the uses of quite poisonous substances to kill or expel intestinal worms without harm to the host. Occasionally with too large doses or when absorption is favored, toxic symptoms may arise in man, which consist of gastro-intestinal disturbances and stimulation of certain parts of the central nervous system, followed by paralysis and death due to depression of the respiratory centre.*

THERAPEUTIC APPLICATION.—The substances of the **Pelletierine** group are employed almost exclusively to remove *tape worms* from the gastro-intestinal tract. In order that an anthelmintic may act successfully, it is necessary that the patient be properly prepared. This **preparation** should begin with the administration of a cathartic and starvation of the patient for twelve to twenty-four hours. The evening before the anthelmintic is to be given, the patient is to eat a little meat well spiced, and with onions. Under these conditions the intestinal tract will be almost empty, so that the worm cannot protect itself in a mass of feces, and the spices and onions will stir up the parasite and thus prevent him from hiding in the rugæ of the intestines. Thus prepared, the anthelmintic is administered in the morning,

followed in a few hours by a purge *The cathartic should not be an oil, as these tend to favor the absorption of the remedies.* If the treatment has been successful, the worm with head will be found in the feces. If the head is not found, the treatment can be repeated in one to two weeks, and best when segments of the worm begin to appear in the feces. The most commonly used *tape worm* remedies are **pelletierine** and **male fern.**

In order to rid the system of *round worms*, the same principle should be employed as with tape worms, i. e., to leave as little residue before the drug is administered as possible, so that it may come into more intimate contact with the parasites. Since round worms occur more frequently in children, and as **santonin,** the best remedy for these, produces disturbances of vision, it is customary to administer the latter at night in order that the child may not be frightened by the coloration of his vision.

MATERIA MEDICA.

Tape Worm Remedies.

Aspidium (U.S.P.), Filix Mas (B.P.), male fern, the rhizome of Dryopteris or Aspidium Filix Mas which grows in America, Asia, Europe and Africa. The main active principle is probably filicic acid, but besides this there are present the neutral bodies aspidin, albaspidin, aspidinin and a fixed oil aspidinol.

Oleoresina Aspidii (U.S.P.) **Dose:**—2.0–4.0 G. Average (U.S.P.), **2.0 G.**

Acidum Filicicum Amorphum, white yellowish powder soluble in cold alcohol. **Dose:**—0.5–1.0 G., given with calomel.

Filmaron, mixture of active principle of male fern occurring in a 10% oily solution under the name of filmaron oil. Dose of latter 10 c.c.

Extractum Filicis Liquidum (B.P.). **Dose:**—45–90 ♏.

Granatum (U.S.P.), Granati Cortex (B.P.). Pomegranate Bark, the bark of the stems and roots of Punica Granatum which grows in the United States and Asia and contains the active alkaloids pelletierine and isopelletierine.

Decoctum Granati Corticis (B.P.). **Dose:**—½–2 fl. ʒ.

Pelletierine. Colorless, oily, aromatic alkaloid, soluble in water, alcohol, ether and chloroform, related chemically to atropine.

Pelletierinæ Tannas, insoluble, tasteless powder. Best preparation because of its insolubility and difficult absorption. **Dose:**—0.2–1.0 G. Average (U.S.P.), **0.25 G.**

Cusso (U.S.P., B.P.) (Kousso or Brayera), female inflorescence of Hagenia Abyssinica, a plant native of Abyssinia. It contains a yellow, amorphous active body kossotoxin and a resinous decomposition product of the latter, kossin. **Dose:**—Average (U.S.P.), **16.0 G.**

Fluidextractum Cusso. **Dose:**—5.0–15.0.

Kamala (U.S.P.), or Rottlera, is a brown powder, consisting of the hair and glands of capsule of the fruit of Mallotus Philippinensis, a plant growing in the Philippines, China and India. It contains two neutral bodies, rottlerin or mallotoxin and kamalin. Dose of Kamala powder, 5.0–10.0.

Pepo (U.S.P.), seed of Cucurbita Pepo or pumpkin. It contains a large quantity of a reddish, fixed oil and also a resin. Powdered seeds are made into a meal. **Dose:**—30–50 G.

Round Worm Remedies.

Santonica (U.S.P.), Levant Wormseed, the unexpanded flower heads of Artemisia Pauciflora, native of Turkestan and contain santonin.

Santoninum (U.S.P., B.P.), colorless to slightly yellow neutral body, almost insoluble in water, more soluble in alcohol. **Dose:**—0.03–0.1 G. Br. (½–2 grains).

Trochisci Santonini (U.S.P.), each containing 0.03. **Dose:**—1–3 troches.

Spigelia (U.S.P.), the rhizome and roots of Spigelia Marylandica, native of the United States and contains a volatile alkaloid, spigeline.

Fluidextractum Spigeliæ (U.S.P.). **Dose:**—1.0–8.0. Average (U.S.P.), 4.0 c.c.

Chenopodium, American wormseed, the fruit of Chenopodium Ambrosioides which grows in the United States and West Indies, and contains as active principle a volatile oil. It is used for the same purposes as santonin.

Oleum Chenopodii (U.S.P.), volatile oil, thin, colorless with a camphorous odor and pungent bitter taste. **Dose:**—0.1–0.5. Average (U.S.P.), 0.2 c.c.

GROUP OF MECHANICAL AGENTS.

The following is a list of substances which are used either for their physical effects in the preparation of active drugs, or for their physical action on some portion of the organism.

Thus the gums, such as acacia, chondrus, althæa and tragacanth, are employed to increase the viscosity of fluid vehicles in order to keep in suspension insoluble substances.

The oils and fats are used to soften the skin, to protect it from the action of air, and to introduce remedies either for it or for the general organisms which are to be absorbed by the skin.

Other substances used to bring remedies in contact with the skin are cotton or solutions of collodion and of gutta percha.

Such substances as sugar, saccharin, rose, melissa, vanilla, raspberries or bayberries are employed to sweeten or flavor medicinal substances or foods.

On the other hand, mulberry juice, saffron and caramel serve to color medicinal preparations.

MATERIA MEDICA.

Acacia (U.S.P.), Acaciæ Gummi (B.P.), or Gum Arabic, gummy exudate from the stem and branches of Acacia Senegal growing in Africa and India. It is composed of whitish opaque masses which fracture like glass, soluble in 2 parts of water, insoluble in alcohol.

Mucilago Acaciæ (U.S.P., B.P.) contains 34 per cent. of gum acacia.

Syrupus Acaciæ (U.S.P.), contains 25 per cent. of the mucilage.

Chondrus (U.S.P.) (Irish moss), an algæ growing on the coast of Ireland and New England. It is composed of dark, purplish, gristly weeds.

Agar-agar, Chinese gelatine or isinglass. It belongs to the same family as the above. It is entirely unabsorbed in the gastro-intestinal tract and has the property of retaining much water. On account of these properties, it has been used with much success in cases of constipation due to too great inspiration of the stools. It is either given plain or in the form of the trade preparation "Regulin" mixed with cereals, apple sauce, soup, etc., at meals.

Althæa (U.S.P.), marshmallow, root of Althæa officinalis.

Syrupus Althææ.

Ulmus (U.S.P.) or slippery elm, the inner bark of Ulmus Fulva.

Mucilago Ulmi.

Tragacanth (U.S.P., B.P.), gummy exudation from Astragalus Gummifer.

Mucilago Tragacanthi (U.S.P., B.P.) contains 6 per cent.

Oleum Olivæ (U.S.P., B.P.), oil expressed from the fruits of Olea Europæa or olives. It is used not only extensively as a food, but as a fattening agent and gentle laxative.

Sapo (U.S.P.), Sapo Durus (B.P.), sodium oleate, made by boiling olive oil with caustic soda. It is the hard Castile soap.

Emplastrum Saponis (U.S.P., B.P.), 10 per cent. soap with lead plaster.

Linimentum Saponis (U.S.P.) (liquid opodeldoc) contains camphor, alcohol, soap, oil of rosemary and water.

Oleum Lini (U.S.P., B.P.), or linseed oil, expressed from the seeds of Linum Usitatissimum.

Sapo Mollis (U.S.P., B.P.), or soft soap, made by boiling linseed oil with caustic potash, and is a soft, brown, yellowish unctuous mass.

Linimentum Saponis Viridis (U.S.P.), contains soft soap, alcohol and oil of lavender.

Linimentum Calcis (U.S.P.) contains olive oil and lime water or carron oil.

Oleum Gossypii Seminis (U.S.P.), or cotton seed oil.

Oleum Amygdalæ Expressum (U.S.P.), Oleum Amygdalæ (B.P.), or oil expressed from the seeds of Amygdalum Communis Dulcis or sweet almonds.

Emulsum Amygdalæ (U.S.P.), 6 per cent. emulsion of almond with sugar and water.

Oleum Theobromatis (U.S.P., B.P.), or cocoa butter, present in the quantity of 50 per cent. in the seeds of the Theobroma Cacao. It is a neutral fat with the odor of chocolate, solid at the temperature of the room, but liquid at the temperature of the body, therefore applicable for the introduction of remedial agents into external cavities of the body, such as the rectum, vagina or urethra.

Oleum Chaulmoogræ, thick brown oil with nauseating odor and taste, obtained from the seeds of Gynocardia odorata. It contains free gynocardic and palmitic acids. Used in the treatment of leprosy both internally

and externally. **Dose:**—Begin with 5 drops and increase to 200 drops 3 to 4 times daily.

Cetaceum (U.S.P., B.P.), or spermaceti, fat extracted from a pocket in the upper jaw of the whale Physeter macrocephalus.

Ceratum Cetacei (U.S.P.) contains 10 grammes of cetaceum to 35 grammes of wax and 55 grammes of olive oil.

Adeps (U.S.P., B.P.), or lard, fat extracted from hogs.

Adeps Benzoinatus (U.S.P.), Adeps Benzoatus (B.P.), lard containing 2 per cent. benzoin.

Ceratum (U.S.P.), lard containing 30 per cent. of wax.

Unguentum (U.S.P.), common ointment, lard containing 20 per cent. of wax.

Unguentum Aquæ Rosæ (U.S.P., B.P.) contains 12½ per cent. of cetaceum.

Oleum Adipis (U.S.P.), oil of lard.

Acidum Oleicum, obtained by the saponification of oil of almonds or of olives. It is a clear, colorless, syrupy liquid used as a solvent for medicine.

Glycerinum (U.S.P., B.P.), triatomic alcohol obtained by the saponification of neutral fats. It is a clear, colorless, odorless, syrupy liquid, with a sweet taste.

Petrolatum, soft paraffin or vaselin, a mixture of hydrocarbons from petroleum. Melting point 45–48° C., used as an emollient and base for ointments.

Petrolatum Album, white petrolatum.

Petrolatum Liquidum, colorless liquid insoluble in H_2O, alcohol; soluble in oils and oil-soluble solvents. Used as a vehicle for sprays, etc.

Gossypium Purificatum (U.S.P., B.P.), the hairs of the seed of Gossypium Herbaceum, or cotton, which is washed to remove the oil. Used in surgical dressings.

Pyroxylinum (U.S.P., B.P.), or gun cotton, made by nitrifying cellulose.

Collodium (U.S.P., B.P.), solution of gun cotton in 3 parts of ether and 1 part of alcohol. Used to cover cuts or to apply remedial agents to the skin.

Collodium Flexile (U.S.P., B.P.), or flexible collodion, same as the above with the addition of turpentine and cotton seed oil.

Collodium Stypticum, collodium containing 25 per cent. tannic acid.

Carbo Ligni (U.S.P., B.P.) (charcoal), made by heating soft wood to a red heat without air. Absorbs gases.

Carbo Animalis (U.S.P.) (animal charcoal), made by burning bones in the exclusion of air.

Carbo Animalis Purificatus (U.S.P.) (purified animal charcoal), made by boiling animal charcoal with hydrochloric acid.

Elastica (U.S.P.), Caoutchouc (B.P.), milky juice from Hevea Brasiliensis or India rubber. It hardens to black balls or cakes, soluble in chloroform, carbon disulphide and benzine.

Liquor Caoutchouc (B.P.) is a 5 per cent. chloroform solution of rubber.

Gutta Percha, exudation from Palaquium Gutta, a plant growing in the Malay Islands.

Liquor Gutta Percha, 9 per cent. solution of gutta percha and chloroform.

Ichthyocolla (U.S.P.), the dried swimming bladders of Acipenser Huso.

Emplastrum Ichthyocollæ (U.S.P.), or court plaster, consists of cloth painted over with a solution of ichthyocolla.

Saccharum (U.S.P.), Saccharum Purificatum (B.P.), or cane sugar, white, crystalline body, soluble in water, insoluble in alcohol.

Syrupus (U.S.P., B.P.), 65 per cent. solution of cane sugar.

Saccharum Lactis (U.S.P., B.P.), or lactose, or milk sugar. White crystalline body, soluble in water.

Mel Despumatum (U.S.P.), Mel Despuratum (B.P.), clarified honey.

Saccharinum, or benzoic sulphinide, a coal tar derivative consisting of white crystals, soluble in alcohol, ether and glycerine, only soluble in 400 parts of water. It is 280 times sweeter than cane sugar. It is used to sweeten the food of diabetics. **Dose:**—0.05 to 0.2 G.

Rosa Gallica (U.S.P.), petals of a species of red rose.

Confectio Rosæ (U.S.P.) contains 8 per cent. rose, besides sugar, honey and rose water.

Oleum Rosæ (U.S.P., B.P.), or attar of rose, pale yellow transparent ethereal oil obtained by the distillation of Rosa Damascus.

Aquæ Rosæ (U.S.P., B.P.) is a saturated, watery solution of oil of rose.

Melissa Officinalis (U.S.P.), a perennial herb growing in Asia Minor and Southern Europe. Contains a volatile oil.

Spiritus Melissæ.

Vanilla (U.S.P.), dark, green climber growing in Mexico and South America and contains the neutral principle vanillin which is a white, crystalline body soluble in ether and alcohol. It can be made artificially from coniferine of pines.

Vanillin. Dose:—0.01 to 0.02 G.

Tinctura Vanillæ contains 10 per cent. of the fruit.

Syrupus Rubi Idæi, 40 per cent. of the juice of rubus idæus or raspberry.

Myrcia or bayberry contains the bay oil.

Spiritus Myrciæ or bay rum.

Succus Mori, mulberry juice.

Syrupus Mori.

Crocus Sativa, or saffron.

Tinctura Croci.

Lycopodium, Spores of Lycopodium, yellow powder used for sprinkling pills.

Amylum, a starch, white powder.

Kaolin, aluminum silicate, insoluble, used as dusting powder.

Talcum, magnesium silicate, insoluble dusting powder.

PART IV.

INORGANIC DRUGS.

Like the organic drugs, the inorganic have both a local and a general action. Although little is known about the manner in which both act, yet with the inorganic we may more frequently observe simpler actions in which we can clearly see a physical process or a fairly simple chemical reaction; thus may be mentioned the "salt action" of sodium chloride on the metabolism, explained by the changing of osmotic tension of the body fluids; the carbonizing effect of sulphuric acid by drawing the water out of the tissues, the local caustic effects of oxidizing agents, free halogens, the alkalies, acids and soluble metals in proper concentration due to the chemical compounds formed between these and the proteids of the cells, thus destroying the vitality of the protoplasm. Another example is the acid intoxication seen in herbivora after feeding on mineral acids. The latter combine with the alkalies in the blood and leave none for the absorption of carbonic acid and the carrying on of internal respiration.

OXIDIZING AGENTS AND FREE HALOGENS.

The local effect is the striking feature and with both oxygen-liberating substances and free halogens there is an oxidation of the living tissues. Halogens combine with the proteids first, but ultimately oxidize and destroy them, just as the pure oxidizing agents. Thus in chemistry we sometimes use for the oxidation of organic matter potassium permanganate or potassium chlorate interchangeably.

GROUP OF OXYGEN.

This group contains oxygen itself and various substances which liberate oxygen when in contact with organic tissues, such as hydrogen peroxide, potassium permanganate, chromic acid, etc., but with all of these except oxygen itself, oxidation takes place only at the site of application, and therefore these oxidizing substances are rather to be considered as local disinfectants, irritants and caustics, than as drugs influencing the internal oxidations.

OXYGEN is absorbed from the air by the alveoli of the lungs. After its absorption it goes into a definite chemical combination with hæmoglobin and only an insignificant portion is dissolved in the serum under normal atmospheric pressure. On account of these facts, its absorption and excretion do not follow the laws of partial tension. The increase or diminution of oxygen in the body, under normal atmospheric pressure, is almost exclusively affected by the increase and diminution of hæmoglobin, by the amount of available breathing space in the lung and by the efficiency of the circulation. All conditions being equal, no more oxygen is taken up by the hæmoglobin when pure oxygen is respired than when ordinary air containing 20 per cent. is breathed. On the other hand, with pure oxygen, the rate of diffusion and absorption being increased, the respiratory frequency is decreased.

Under normal atmospheric pressure the inhaling of undiluted oxygen increases the quantity of the same dissolved in the plasma from the normal 0.6 per cent. to 3 per cent. When it is administered under increased pressure, the augmentation in the quantity dissolved in the serum may be sufficient so that this portion alone is capable of maintaining life, if the pressure is high enough.

OZONE is a much more active oxidizing agent than oxygen. It is a powerful *irritant* and *disinfectant*. When breathed, it produces severe irritation of the **respiratory passages,** being capable of causing death by inflammation of the lungs. The quantity present at times in air is, however, too slight to produce any symptoms.

HYDROGEN PEROXIDE liberates oxygen slowly in the air, but rapidly when in the presence of animal or vegetable tissues, such as blood, various organs, pus, bacteria, etc. Because of this oxygen it is a strong oxidizing agent and, therefore, a disinfectant because it destroys the bacteria and the food on which they live.

When hydrogen peroxide is applied to a **mucous membrane** or to a wound, especially when blood or pus is present, it foams violently and produces a burning sensation. The oxygen thus liberated is not appreciably absorbed by the circulation, so that the internal administration of hydrogen peroxide cannot increase the oxygen in the blood. If introduced intravenously, or subcutaneously, or into serous cavities, it may produce oxygen emboli in the circulation with fatal consequences.

Lately there have been introduced a number of other inorganic peroxides, as those of **sodium, magnesium** and **zinc,** also the organic **benzoyl acetyl peroxide.** These do not give up their oxygen as readily as hydrogen peroxide, yet have quite well-marked disinfectant properties.

POTASSIUM PERMANGANATE also liberates nascent oxygen when in contact with organic tissues. Because of this nascent oxygen which combines with the proteids, it acts in strong solutions as a caustic, especially over raw surfaces and **mucous membranes,** and in dilute solutions as an irritant. The lower fungi or bacteria are killed and therefore it is an antiseptic. Its effect is very superficial because it becomes reduced to an inactive state before it can penetrate deeply into the tissues. For this reason it cannot increase the oxygen contents of the blood or act in the circulation as a disinfectant, as it is destroyed by reduction before it is absorbed. Although recommended to destroy poisons in the stomach and intestines, it has little such action, for it loses its activity in contact with the mucous membranes lining the canal leading to the gastro-intestinal tract.

When taken internally in sufficient quantities, the **symptoms of poisoning** consist of those of gastro-enteritis, such as nausea, vomiting, diarrhœa and collapse. When locally applied, it stains

the skin brown because of the reduction of the permanganate to the black oxide of manganese. This discoloration can be easily removed by washing with a solution of oxalic acid.

CHROMIC ACID and **POTASSIUM BICHROMATE** in common with other substances of this group easily give up nascent oxygen to organic tissues, but in addition they have a constitutional action due to the metal chromium. Chromic acid is especially caustic because its oxidizing properties are reinforced by its acid constitution. Both the bichromate and the acid act as **irritants** and **antiseptics,** and in solutions of great concentration, as **caustics.** Their corroding effect is great, but less painful than that of most other caustics, although they are sometimes dangerous from the extreme poisonous effect of chromium after absorption.

The **symptoms of poisoning** consist of diarrhœa, vomiting, albuminuria, hematuria, fall of blood pressure, muscular twitching and even convulsions. On pathological examination, there is great congestion of the gastro-intestinal tract, frequently accompanied by ecchymoses and ulcerations. The kidneys are in a state of acute nephritis. The symptoms referable to the gastro-intestinal tract and kidneys are due to the fact that chromium is excreted by these organs, mainly by the latter. Chronic poisoning occurs in factories, and consists of ulcerations in the nose and ears, chronic inflammation of the larynx and pharynx, due to the inhalation of chromate dust. When given to animals over a space of time, they may produce chronic interstitial nephritis.

SUMMARY OF GROUP ACTION.—*Oxygen normally acts as the oxidizer of food stuffs to furnish heat and force. It cannot be increased in the blood by increasing its concentration in the air unless the atmospheric pressure is also increased. Only a decrease in the rate of respiration occurs when more concentrated oxygen is inhaled. The other members, as Hydrogen Peroxide, Potassium Permanganate, etc., have no effect on internal respiration, but act only locally as oxidizing agents, disinfectants, irritants and caustics.*

THERAPEUTIC APPLICATION.—Pure **oxygen** is used in medicine in diseases of the respiratory tract attended by dimin-

ished lung capacity, as in *pneumonia* or *phthisis*, also in extreme dyspnœa from *cardiac insufficiency*. Its good effect, if any, in these cases is to be referred to the diminution of the dyspnœa of the patient on account of the more rapid rate of absorption of oxygen. The latter is used mixed *with anæsthetics* in order to diminish danger from asphyxia. It might be useful in cases of *poisoning with carbon monoxide* and the poisons which produce methæmoglobinæmia, if given under sufficient pressure to dissolve 20 per cent. in the plasma and replace the functions of the crippled hæmoglobin. **Hydrogen peroxide** is used in a 3 per cent. solution as a disinfectant and to *cleanse wounds*. It should never be injected into closed cavities without outlet, or into blood vessels, on account of the danger of local pressure in one case and formation of emboli in the other.

Potassium permanganate is also used as a disinfectant for washing surgeons' hands, for *irrigating infected canals or cavities*, as in *gonorrhœal urethritis* and *vaginitis*, and in diseases of the mouth and rectum. This substance and hydrogen peroxide have been used in the past subcutaneously or internally in cases of poisoning with the hope that the poison might be more rapidly oxidized. The fallacy of this administration is obvious from the pharmacological action. It may, however, be of value when injected around and in the site of a *snake bite*, also when the wound is enlarged surgically and washed with strong permanganate solutions.

Chromic acid, in concentrated form, is used mainly as a local *caustic* to burn off new growths, etc. In dilute solutions this acid and the bichromate of potassium are sometimes employed as disinfectants.

MATERIA MEDICA.

Aqua Hydrogenii Dioxidi (U.S.P.), Liquor Hydrogenii Peroxidi (B.P.), is a 3 per cent. solution of hydrogen dioxide in water. It is a colorless, odorless, acid liquid which foams when in contact with pus or other organic material. Used as a disinfectant wash for wounds or external cavities of the body, such as the mouth. **Dose:**—Average (U.S.P.), **4.0 c.c.**

Potassium Permanganas (U.S.P., B.P.) is composed of small purplish crystals with a sweetish, astringent taste, soluble in 16 parts of water. It imparts to water even in very dilute solutions a deep pink or red color. It

easily liberates oxygen when in contact with organic material. **Dose:**—0.05 to 0.2 G. Br. (1–3 grains). Average (U.S.P.), **0.065.**

Acidum Chromicum (B.P.), dark red crystals, very lustrous and deliquescent, soluble in 10 parts of water. It oxidizes organic material with readiness. Used externally as a caustic.

Potassii Bichromas (B.P.), large, orange red crystals having a bitter metallic taste, soluble in 10 parts of water. **Dose:**—0.005 to 0.01 G. Br. ($\frac{1}{10}$–$\frac{1}{5}$ grain). Average (U.S.P.), **0.01 G.**

GROUP OF FREE HALOGENS.

This group comprises the free halogens, Chlorine, Bromine, Iodine, and those compounds of these from which they are easily liberated in the free state.

The free halogens form insoluble compounds with proteids which later become dissolved and destroyed. Their effects on the latter may be explained firstly by their entering the proteid molecule, secondly by withdrawing hydrogen to form an acid, and lastly by breaking up the water in the tissues and forming nascent oxygen. On account of this action they act as irritants, caustics and disinfectants. These properties are most marked with chlorine, less marked with bromine, still milder with iodine.

When **CHLORINE** is kept on the skin the destruction is terrific, but it is as well marked with **BROMINE**; the latter being a liquid, remains longer in contact with the tissues and penetrates deeply into these, thus in a few minutes after application the most widespread destruction of living matter may take place and the ulcers left by this corrosion are always slow to heal, probably because the disabling effect reaches into the remaining living tissues. **IODINE** is much less caustic, and even in ten per cent. solution on the skin it only causes a little burning and itching, but when the brown color of the iodine disappears the skin usually looks red and peels. Strong solutions may act as a caustic on mucous membranes and always produce an inflammatory reaction.

Chlorine gas, by combining with hydrogen sulphide and ammonia, destroys the odor of these and of other bad-smelling gases; thus it acts as a deodorizer.

When **chlorine** and **bromine** vapors are breathed they produce

severe irritation of the eyes, nose and throat, bronchi and lungs, which may well result fatally from œdema of the larynx or pneumonic inflammation. Even small quantities, as one part of chlorine and bromine in a million of air, produce terrible burning pain in the eyes, nose, throat and chest, with sneezing and violent coughing. Severe bronchitis or pneumonia with hemorrhage from the lungs are frequent sequels of inhaling the halogen fumes. Unconsciousness usually supervenes early.

When the halogens are taken internally in large quantities, death takes place from *gastro-enteritis and collapse.* They produce severe pain in the throat, œsophagus and abdomen, with bloody vomiting and diarrhœa if death does not take place immediately. If the quantity taken is not sufficient for fatal results, they cause ulcerations at the place of contact, especially along the œsophagus and **stomach.** If death does not result within a few days from perforation of these ulcers, the latter heal with the formation of cicatricial tissue, which in the œsophagus or at the openings of the stomach may produce stenosis and occlude the passage along the gastro-intestinal canal. In case of poisoning by swallowing chlorine and bromine, the chemical antidote is albumin, while with iodine it is starch.

Chlorine and bromine are said to have specific **narcotic properties:** in factories, workmen poisoned by the halogen fumes frequently show symptoms of somnolence and dulled intellect. The vapors of **iodine** are also irritant when inhaled, but are not so severe as those of chlorine and bromine. The quantity of fumes liberated from iodine at the ordinary temperature is so small that it takes quite prolonged inhalation to get reddening of the eyes, sneezing with watering of the nose, and coughing with pain in the chest. When taken by the stomach in even small doses, iodine causes vomiting, nausea, often tenderness of the abdomen and diarrhœa. With large quantities, the symptoms are those of severe acute gastro-enteritis, as from any irritants. The irritation of the gastro-intestinal tract is not only observed by internal administration but also after subcutaneous application, injections into tumors or sacs, or into the uterus; it

may be explained by the excretion of this halogen by the salivary glands and stomach.

Iodine is probably absorbed chiefly as an albuminous compound: it circulates through the body as such and is excreted in main part by the kidneys in the form of iodides. Small amounts, however, are excreted by the mouth, upper respiratory tract and skin, probably in the form of a loose albuminous compound. The irritation of the skin and respiratory passages which occurs in **iodism** can be explained by the liberation of iodine from the secretion of these organs. It is also excreted by the stomach in the form of hydriodic acid which becomes partly decomposed into iodine.

Occasionally when iodine is given in small doses to a patient over a period of time, besides evidences of local irritation there is observed a marked change in the metabolism. The patient loses weight, his pulse becomes accelerated, he grows very nervous, irritable and sleepless and may show fine tremors of the extremities. These symptoms are the same which may be observed after an overproduction of thyroid extract or in exophthalmic goitre and may be due to the stimulation of that gland, which itself contains much iodine. Besides these there may occur atrophy of the breasts and testicles, but skin eruptions and irritation of the respiratory tract are rare, therefore this form of chronic action of iodine is quite different from that of iodides.

Though rare, even **fatal poisoning** has resulted after the absorption of iodine by cysts. The symptoms were sleepiness, thirst, constant vomiting, sensitiveness of the abdomen, cyanosis of the cheeks and extremities, small weak pulse, skin eruptions and death in a few days. After death in man, the mucous membrane of the gastro-intestinal tract shows marked inflammation, and in animals even fatty degeneration of the parenchymatous organs has been observed.

SUMMARY OF GROUP ACTION.—*Local irritants, caustics and disinfectants through their action on proteids Poisoning by inhalation gives terrific inflammation of the respiratory tract, while that by ingestion produces widespread destruction of the alimentary canal.*

THERAPEUTIC APPLICATION.—The use of the halogens in medicine is based almost wholly on their local action. Chlorine, bromine and iodine in the form of pastes have been used, especially by so-called "cancer specialists," as caustics to burn off *superficial cancers*. **Iodine** solutions are used as *disinfectants* and *astringents* in wounds or diseased cavities such as that of the uterus, nose and throat; also as local irritants to produce adhesions of the walls of a *hydrocele* by inflammatory reactions; also employed as *counterirritants* in painful or inflammatory affections of the chest and joints.

Chlorine water and solutions of iodine were formerly used internally as disinfectants of the gastro-intestinal tract in such infectious conditions as *typhoid fever*. Nowadays, we still use externally to disinfect wounds the solution of **sodium hypochlorite,** which contains and acts by virtue of its free chlorine.

Chloride of lime, which gives off chlorine by the influence of carbon dioxide, is used as a *deodorizer* in sick rooms, water closets, etc., also as a disinfectant of infectious urines, stools, etc.

MATERIA MEDICA.

Aqua Chlori, a clear, greenish-yellow liquid with the suffocating odor of chlorine. It is a 0.4 per cent. solution of chlorine gas and water. **Dose:**—5 to 15 c.c.

Calx Chlorinata (U.S.P., B.P.), or chlorinated lime, or calcium hypochlorite, is a grayish-white powder with the odor of chlorine. It is gradually decomposed by the carbonic acid of the air with the liberation of chlorine. It should contain 35 per cent. of available chlorine.

Liquor Sodæ Chlorinatæ (U.S.P., B.P.) or Labarraque's solution. It is a solution of chlorinated soda containing at least 2½ per cent. of available chlorine and is a pale green liquid with the odor of chlorine. **Dose:**—0.5 to 1 c.c. Br. (3–15 ♏). Average (U.S.P.), **1.0 c.c.**

Bromum (U.S.P.), dark, fuming, brownish-red liquid, soluble in 30 parts of water, more readily soluble in water containing potassium bromide. Easily soluble in alcohol and ether.

Iodum (U.S.P., B.P.), heavy bluish crystals with a metallic luster, penetrating odor and burning metallic taste. Soluble in 5,000 parts of water. Easily soluble in water containing potassium iodide. Soluble in 10 parts of alcohol and freely in ether.

Tinctura Iodi (U.S.P.), 7 per cent. solution of iodine and alcohol. **Dose:**—0.1 to 0.5 c.c. Average (U.S.P.), **0.1 c.c.**

Tinctura Iodi (B.P.), 2½ per cent. solution. **Dose:**—2–8 ♏.

Liquor Iodi Compositus (U.S.P.) or Lugol's solution, contains 5 parts of iodine, 1.0 of potassium iodide to 100 of water. **Dose:**—0.2 to 1.0 c.c.

Unguentum Iodi (U.S.P., B.P.) contains 4 per cent. iodine besides potassium iodide and benzoinated lard.

Iodopine, compound of iodine with fats. Used internally in place of iodine or iodides.

Iodoformum (U.S.P., B.P.), yellow crystals, nearly insoluble in water, soluble in alcohol, ether and fats, with intensely disagreeable odor. Liberates iodine in contact with wounds or fluids of the body. Causes at times after absorption from wounds or too large internal doses, delirium and mania and even death in collapse. Used as an antiseptic dusting powder, injected in oily solution into tuberculous joints, also internally for treatment of syphilis on account of its iodine. **Dose:**—0.03 to 0.2 G. Average (U.S.P.), **0.25 G.**

Iodoformum Aromatisatum, same as above, flavored with 4% cumarin.

Iodolum, tetraiodopyrrol, grayish-brown crystals insoluble in water. Does not smell as badly as iodoform. Uses and dose same.

GROUP OF WATER.

The action of water is complicated by its temperature and by the salts which it always contains except when distilled.

Since three-quarters of the bulk of a living organism is composed of water, we would not expect a marked action from the administration of small quantities, yet it has certain properties of interest.

Distilled water is an irritant poison. This irritation is produced by its power of extracting salts from the living tissues with which it comes in contact. In this way small animals, amœbæ, fish, etc., are killed. It is irritating to sensitive mucous membranes, as those of the nose, and also to denuded surfaces. Taken over a prolonged period of time, it may produce gastro-enteric inflammation, and by diminishing too much the salt concentration of the urine, it may even produce irritation of the kidneys. It is not absorbed from the unbroken skin.

Ordinary water is also not absorbed from the unbroken skin. After long-continued baths the superficial layers of the epidermis may imbibe a small quantity, which, however, does not reach the circulation.

Water is not absorbed from the stomach, but easily so from the intestines, and most readily if taken before meals when the latter tract contains the least solid material.

The ingestion of large quantities of water may increase the

number of stools and their watery contents. It increases the excretion of urine and often of sweat.

Inhalation of watery vapors may cause dyspnœa, headaches, dizziness, great congestion of the head and even apoplectic attacks. This action is probably due mainly to reflex stimulation of the vasomotor centres by the temperature.

On account of the increase in absorption and excretion which it causes, water augments the interchange of material in the body and, therefore, the metabolism. This leads to a greater excretion of urea and sulphates. The body learns to accommodate itself to the new condition and in a few weeks the nutrition becomes normal.

Mineral waters possess merely the action of ordinary water plus that of the salts which they contain. The action of the latter will be described in another group.

THERAPEUTIC APPLICATION.—Water is used externally in the form of baths in various *skin diseases* to soak off scales or crusts on the upper layer of the epidermis, and prepare the skin for the action of other agents, such as the salts contained in the water itself.

It is used in the form of *poultices* to soften the epidermis and allow the easy escape of pus from an abscess. The heat of poultices is also employed as a counterirritant to influence internal pain.

Cold baths, which act by virtue of the temperature, are used in various chronic diseases as reflex stimulants of respiration, circulation and general metabolism. They are also employed in fevers to decrease the body temperature.

Hot baths are especially useful to produce sweating and rid the body of undesirable products, as in Bright's disease, acute infections, colds, rheumatism and gout.

Local hot baths are used on the feet to congest the latter and to draw the blood away from inflamed internal organs, as lungs or brain.

Hot sitz baths are used to congest the pelvic organs and restore suppressed menstruation.

The sweating seen after hot or cold baths is not due to absorption of water from the bath, but probably to the hyperemia of the skin brought about by the temperature changes and to some extent by retention of water in the blood, and inbibition in the epidermis during the bath.

The quieting influence which warm baths have on the central nervous system is sometimes used to relieve restlessness, pain and muscular spasm.

Water is used at spas for the treatment of almost every chronic disease. Its good effects are probably mainly due to its power of increasing general metabolism. It is serviceable as a diuretic in *kidney disease* and to prevent the formation of *stones* in the kidney and bladder. It is also employed in *constipation* and catarrh of the small intestine.

The quantity of water ingested is restricted in diarrhœa. It was formerly decreased in dropsies in order to make the blood more concentrated and aid absorption of fluid. By its diminution in obesity, the absorption of food may be hindered and thus body weight may be reduced.

Water is used to distend the rectum in the form of clysters and thus reflexly produce an emptying of the bowels. The drinking of large quantities at one time may, by distending the stomach, produce vomiting.

GROUP OF ACIDS.

The members of this group are all the inorganic and organic acids which act by virtue of their acid structure and properties, and not in a specific way as do hydrocyanic and arsenious acids. For in the two latter the specific action entirely obscures the general acid action.

The stronger mineral acids, such as sulphuric, hydrochloric, nitric and phosphoric *precipitate, then destroy proteids in concentrated solutions*, but *merely dissolve them in dilute ones, forming acid albuminates.* They change the composition of the tissues of the body by withdrawing their water. Concentrated **SUL-**

PHURIC ACID acts so energetically in this direction that it not only removes the preformed water, but breaks up the organic material by forming water from the hydrogen and oxygen, leaving ultimately nothing but carbon. When applied to the skin, it produces at first a white eschar due to precipitated proteid which turns black by carbonization. The destructive action of **NITRIC ACID** on proteids is due in good part to the formation of a nitro-derivative, xanthoproteic acid, which is later oxidized, when complete destruction of the proteids occurs. The eschar on the skin is yellow, due to the color of the xanthoproteic acid. **HYDROCHLORIC ACID** is less likely to cause deep-seated corrosion and attacks chiefly the superficial layers of the skin and raises blisters. **PHOSPHORIC ACID** is a still milder caustic. Most organic acids have a mild effect, but some, such as **glacial acetic, trichloracetic** and **lactic,** have a caustic action, only much weaker than the inorganic. All except sulphuric and nitric produce a white eschar. With acids, *the caustic effect has a tendency to limit itself because of the wall of precipitated proteids* which is formed to check the advance of the agents. This makes their local action different from that of the caustic alkalies which do not precipitate proteids and have the tendency to spread deeper and deeper without limits.

In dilute solutions the members of this group attack proteid substances forming albuminates and thus are *irritants and antiseptics*. The amount of irritation and antiseptic action depends upon the strength of the particular acid and its concentration. As almost all living tissues have an alkaline reaction, acids destroy their life and act in a sense as protoplasmic poisons. An apparent exception seems to be a few moulds and other lower forms which live in acid solutions, e. g., the Sarcinæ found in the stomach in dilatation of this organ. Most bacteria, however, are killed by even as low a concentration as 0.2 per cent. hydrochloric, the quantity found in the normal stomach of man.

The **symptoms** of acute corrosive poisoning by strong acids are those of *gastro-enteritis*, with intense pain in the mouth, œsophagus and stomach, vomiting and often diarrhœa, profound

shock, weak pulse and respiration. Death occurs from collapse due to the severity of the gastro-intestinal lesion, which, with the stronger acids, may amount to perforation. When a patient passes the acute attack, he frequently suffers from narrowing of various parts of the tract due to cicatricial contraction of the ulcers. The treatment of this corrosive poisoning is based on the neutralization of the acid by dilute alkalies. Those which of themselves are not corrosive and which do not produce gas, as magnesium oxide, are best adapted. After the ingestion of fuming acids or the inhalation of fumes of nitric or hydrochloric, death may take place immediately from œdema or spasm of the glottis. If the subject survives long enough, he may later die of pneumonia.

Besides the corrosive form of poisoning, another may be seen in herbivorous animals after internal administration of dilute acids. This is the so-called **"acid-intoxication"** which is due to the diminution of the alkalinity of the blood incident to the combination of the absorbed acid with its fixed alkali and the excretion of the resulting compound. Thus, as the alkalinity of the blood becomes lowered, less and less carbon dioxide is absorbed from the tissues, and in consequence of this diminution of internal respiration the animal dies from asphyxia before the blood becomes acid or even neutral. The symptoms consist, at first, of deep gasping respirations (air hunger), which afterwards become shallow and superficial until they stop entirely. The heart grows progressively weaker and consciousness is gradually lost.

After internal administration of acids this intoxication is not seen in men or dogs. The probable explanation is that these animals, being carnivorous, have a protective metabolism against acid-intoxication. Since their food, meat, gives rise to the formation of much acid, and since they do not take, as herbivorous animals, large quantities of alkaline salts in their diet, their bodies easily form the alkali ammonia which neutralizes the acids ingested or produced by their metabolism. These are excreted, in carnivora, mainly as ammonium compounds. The increase

in the ammonia excretion after the administration of acids is at the expense of the urea which is correspondingly diminished.

Acid-intoxication may also be produced in carnivorous animals by intravenous or subcutaneous injections of acids, thus introducing larger quantities than they can neutralize. A typical acid-intoxication is seen in man at the end of the disease diabetes. In this condition oxybutyric and diacetic acids are formed so rapidly that the protective mechanism is insufficient to neutralize them, although enormous quantities of ammonia are found in the blood and urine. Sometimes as much as 140 grammes of acids have been recovered from the body in twenty-four hours, just before death in diabetic coma; it is not surprising under such circumstances that ammonia cannot be manufactured rapidly enough.

The **excretion** *of acids takes place by the kidneys in herbivora in the form of salts of potassium, in carnivora chiefly of salts of ammonia;* but the body tries to retain all the alkalies possible and throws them out in the form of acid salts and occasionally as free acids. These may markedly irritate the kidneys so that albumen, casts and blood may be present in the urine. They may cause pain over the bladder and a burning feeling during urination due to irritation of the bladder and urethra.

The **ORGANIC ACIDS,** as acetic, citric, lactic and tartaric, are absorbed as salts of the alkalies and during their passage through the body are in most part **oxidized** *to carbonates and* **excreted** *as such by the kidneys*, so that after internal administration they do not decrease the alkalinity of the blood nor do they make the urine more acid.

As mentioned before, many of the organic acids are also very irritating in concentrated form, but when diluted they exert only gentle stimulant action, which when taken internally may help to remedy dryness of the mouth and to quench thirst by stimulating the mucous secretions and saliva. Externally, in the form of vinegar rubs, they may stimulate the skin, cause sweating, and reflex stimulation of the **central nervous system and circulation.**

CARBONIC ACID is one of the weakest, possessing only mild irritant properties. Yet when inhaled in concentrated form, it is capable of producing a reflex spasm of the glottis.

When applied to **mucous membranes** or denuded surfaces, it produces at first a sensation of burning, then one of numbness or local anæsthesia.

Taken internally, it probably increases reflexly the flow of the digestive juices. It augments markedly the absorption of water from the **intestines** and consequently the excretion through the **kidney.** It also aids the absorption of alcohol by the stomach.

When breathed, carbonic acid first stimulates the **central nervous system,** producing deeper breathing. This is followed by depression with hypnosis and death from paralysis of respiration. Its constitutional action is not seen after ingestion, because very little is absorbed and it is quickly **excreted** by the lungs.

SUMMARY OF GROUP ACTION.—*Action due to acid constitution. Caustics and irritants, in concentrated form. Stimulants and antiseptics, in diluted form. Poisoning by internal administration of strong concentrated acids, gastro-enteritis. In herbivora by ingestion and in carnivora by intravenous injection, acid intoxication with decrease in alkalinity of the blood, diminution of the power of taking up carbon dioxide from the tissues and death from asphyxia.*

THERAPEUTIC APPLICATION.—The stronger acids, especially **nitric, glacial acetic** and **trichloracetic,** are used as caustics to burn off *epitheliomata, chancres* and *gangrenous ulcers.* They were also formerly frequently employed as hemostatics.

Dilute acids, as **acetic,** are used externally and by inhalation to *reflexly stimulate the central nervous system.*

Citric acid is given in the form of lemonade in fevers to reflexly stimulate salivary secretion, and thus relieve *dryness of the mouth.*

Dilute mineral acids, especially **hydrochloric,** are used to replace deficiency in the normal acidity of the stomach and thus to help the pepsin to carry on *digestion.* Mineral acids should

always be given through a glass tube to prevent destruction of the teeth.

Acids, especially dilute organic, as vinegar, are useful *antidotes in cases of alkali poisoning.*

Hydrochloric acid, which acts as the normal *antiseptic* of the stomach, is sometimes used to prevent certain forms of fermentation in the latter.

Boric acid, although very weak, is often employed as an antiseptic wash in the nose, throat, mouth, vagina, rectum, ear, etc.

Carbonic acid has been used in the form of baths as a *reflex stimulant* to the central nervous system, circulation and metabolism. Taken internally, it also increases the nutrition through the larger absorption of water which it produces.

On account of its local anæsthetic action, it was formerly used to wash wounds. It is now given in the form of sparkling drinks as soda water or champagne to check pain in the stomach and nausea or vomiting in seasickness and pregnancy.

MATERIA MEDICA.

Acidum Sulphuricum (U.S.P., B.P.), a colorless, oily liquid containing not less than 92½ per cent. by weight of sulphuric acid.

Acidum Sulphuricum Dilutum (U.S.P., B.P.) contains 10 per cent. by weight of sulphuric acid. **Dose:**—0.5 to 2.0 c.c. Br. (10–30 ♏). Average (U.S.P.), **2.0 c.c.**

Acidum Sulphuricum Aromaticum (U.S.P., B.P.) contains 20 per cent. by weight of sulphuric acid besides oil of cinnamon, tincture of ginger and alcohol. **Dose:**—0.3 to 1.0 c.c. Br. (8–15 ♏). Average (U.S.P.), 1.0 c.c.

Acidum Nitricum (U.S.P., B.P.), colorless, fuming liquid containing 68 per cent. by weight of nitric acid.

Acidum Nitricum Dilutum (U.S.P., B.P.) contains 10 per cent. by weight of nitric acid. **Dose:**—0.5 to 2.0 c.c. Br. (10–20 ♏). Average (U.S.P.), **2.0 c.c.**

Acidum Nitrohydrochloricum (U.S.P.) contains 18 parts of nitric acid and 82 parts of hydrochloric acid.

Acidum Nitrohydrochloricum Dilutum (U.S.P.) contains 4 parts of nitric acid, 18 of hydrochloric, and 78 of water. **Dose:**—0.5 to 2.0 c.c. Average (U.S.P.), **2.0 c.c.**

Acidum Hydrochloricum (U.S.P., B.P.), colorless, fuming liquid containing 31.9 per cent. of hydrochloric acid.

Acidum Hydrochloricum Dilutum (U.S.P., B.P.) contains about 10 per cent. hydrochloric acid. **Dose:**—0.5 to 2.0 c.c. Br. (10–30 ♏). Average (U.S.P.), **1.0 c.c.**

Acidum Phosphoricum (U.S.P., B.P.), colorless liquid containing 85 per cent. by weight of absolute orthophosphoric acid.

Acidum Phosphoricum Dilutum (U.S.P., B.P.) contains 10 per cent. of orthophosphoric acid. **Dose:**—0.5 to 2.0 c.c. Br. (10–30 ♏). Average (U.S.P.), **2.0 c.c.**

Acidum Aceticum Glaciale (U.S.P., B.P.) contains at least 99 per cent. absolute acetic acid.

Acidum Aceticum (U.S.P., B.P.), colorless liquid, having the smell and taste of vinegar, contains 36 per cent. by weight of absolute acetic acid.

Acidum Aceticum Dilutum (U.S.P., B.P.) contains 6 per cent. acetic acid. **Dose:**—5.0 to 15.0 c.c. Br. (1–4 fl. ʒ). Average (U.S.P.), **2.0 c.c.**

Acidum Trichloraceticum, colorless, deliquescent crystals, soluble in alcohol and ether, decomposed by heat in the presence of sodium carbonate into chloroform.

Acidum Citricum (U.S.P., B.P.), colorless crystals, very soluble in water. **Dose:**—0.5 to 2.0 c.c. Br. (3–30 grains). Average (U.S.P.), **0.5 G.**

Syrupus Acidi Citrici (U.S.P.) contains 1 per cent. citric acid. **Dose:**—5.0 to 15.0 c.c.

Acidum Tartaricum (U.S.P., B.P.), colorless crystals, easily soluble in water, soluble in 2½ parts of alcohol. **Dose:**—0.5 to 2.0 G. Br. (5–20 grains). Average (U.S.P.), **0.5 G.**

Acidum Lacticum (U.S.P., B.P.), colorless, syrupy liquid, containing 75 per cent. by weight of absolute lactic acid. **Dose:**—0.5 to 2.0 c.c.

Acidum Boricum (U.S.P., B.P.), colorless crystals with a slightly bitter acid taste, soluble in 25 parts of water, in 10 of glycerine and 15 of alcohol. **Dose:**—0.5 to 2.0 G. Br. (5–15 grains). Average (U.S.P.), **0.5 G.**

Glyceritum Boroglycerini (U.S.P.), Glyceritum Acidi Borici (B.P.), contains 31 per cent. of boric acid.

GROUP OF ALKALIES.

Just as the members of the previous group contain substances which act only through their acid properties, so those of this division have little or no other action, except that imparted to them through their **basic nature.** Such basic bodies as the alkaloids with a marked special effect are excluded.

The stronger members, **SODIUM** and **POTASSIUM HYDRATE** and **CALCIUM OXIDE** *in concentrated form act as powerful caustics.* This effect is due partly to the withdrawing of water, as in the case of the acids, and partly by the transformation of the proteids into soluble alkali albuminates, by the solution of connective tissue and saponification of the fats. Since the products of this caustic action are soluble, there is a great tendency for diffusion and deep-seated destruction, so that here lies an essen-

tial difference between caustic action by alkalies and by acids, the latter having the tendency only to produce localized destruction, because they coagulate the proteids. With alkalies, as with most other chemical caustics, everything is destroyed with which they come in contact, including skin, muscle, vessels, nerves and new growths. The corrosive effect here is also attended by inflammatory reaction at the boundary between the destroyed and living tissues.

Taken internally in concentrated form, the **symptoms** are those of *gastro-enteritis* with a greater tendency to perforation than with strong acids. There is great pain in the mouth, throat, œsophagus and stomach with vomiting and frequently diarrhœa, also early symptoms of collapse especially if perforation has occurred. The burned **mucous membrane** is soft, slimy and mushy after caustic alkali poisoning, while it is tough and puckered after burning with acids.

In dilute solution, the caustic alkalies act only as local irritants, the amount of irritation varying with the concentration. Even in dilute solutions, albumins are transformed to alkali albuminates. The skin after topical application is first entirely cleansed of the oil and dirt, then the superficial layers of the epidermis are dissolved, when it becomes reddened and irritated. In the mouth, there is the typical "lye taste" and a solution of the superficial layers of the mucosa, while the latter is bright red and feels slippery. Dilute alkalies in the stomach neutralize the normal hydrochloric acid and interfere with the digestion of proteids if the secretion is normal, but may aid the symptoms of hyperacidity if the latter is present. They were formerly thought to exercise a stimulant action on gastric secretion, but experiments seem to show that they decrease hyperacidity when given over a prolonged period of time. In the **intestines** they may neutralize an excess of acid coming from the **stomach.** They dissolve the **mucus** in catarrhal conditions, but have no influence on the secretion of bile.

The weaker members of the group, such as the **CARBONATES, BICARBONATES** and **PHOSPHATES,** do not act as caustics,

but only as irritants. *They may dissolve the superficial layers of the epidermis, but do not produce deep destruction.*

MAGNESIUM OXIDE is practically insoluble in water and possesses no irritant properties. When administered internally, it neutralizes the hydrochloric acid in the gastric juice and on reaching the intestine, by virtue of the specific action of the magnesium ions on the intestinal mucosa, it sets up the reflex which causes increased peristalsis and a laxative effect.

The hydrates *are probably* **absorbed** *as carbonates or as alkali albuminates.* They become saturated with carbon dioxide in the blood and are **excreted** in this combination by the kidneys and possibly by the respiratory mucous membranes.

All alkalies are readily excreted, so that the increase in alkalinity of the blood is never very great, although when abnormally large quantities of acids are formed in the system, as in diabetes, they may protect the organism from acid-intoxication. On account of their excretion by the **kidneys,** they make the urine alkaline or less acid, and increase the total secretion. By their probable excretion on the **bronchial mucous membrane,** they are said to act as expectorants and in pathological conditions to render the mucus less tenacious and more easily expelled.

There is a small increase in **metabolism** which, if not due to the augmented alkalinity of the blood, can be explained by salt action and the greater interchange of fluids in the tissues. The total nitrogen in the urine is not much affected, but its form is changed, as the ammonia is decreased with a corresponding increase in the urea. The uric acid excretion varies, sometimes being augmented and at other times diminished. French authors believe that alkalies produce a retention of water in the body due to the retention of chlorides which follows their use and that actual œdema may follow the use of too great quantities of sodium bicarbonate. An opposite view is held by some workers in this country, who believe, on the contrary, that acidity of tissues due to stasis causes œdema, while alkalinity prevents this result.

The bicarbonates and phosphates of the alkalies, as also mag-

nesium oxide, are not quickly absorbed, so they possess in addition *a laxative effect* due to their local action on the intestines.

SUMMARY OF GROUP ACTION.—*Action through the basic ions on account of their power of neutralizing acids and dissolving proteids. Caustics in great concentration. Irritants, stimulants and solvents for mucus in diluted solutions. Absorbed as alkaline carbonates and albuminates. Excreted as carbonates by the urine. Temporary increase in the alkalinity of the blood. Poisoning from concentrated solutions consists of acute gastro-enteritis.*

THERAPEUTIC APPLICATION.—The **caustic alkalies** are used in medicine to burn off *new growths* and other undesirable products of disease. After such application the surrounding tissues should be washed with dilute acids to prevent too great spreading.

In the form of **bicarbonate** or **phosphate of sodium,** alkalies are useful to dissolve the mucus in *catarrh of the stomach.* They are of value in neutralizing an *excessive secretion of hydrochloric acid.* They are also employed in cases of *acid poisoning.* For this purpose **hydrates** or **oxides** are preferable to carbonates because no gas is liberated which might distend the stomach. The alkali oxides or hydrates may also be used in dilute forms to take up an excess of carbon dioxide gas in the stomach or intestines.

The alkalies are used especially in the form of mineral waters in the treatment of diseases with faulty metabolism, as *gout, rheumatism* and *diabetes.* But in the latter they are strongly indicated at the approach of coma due to *acid-intoxication* when sodium bicarbonate is given not only internally but also subcutaneously or intravenously. By the latter method, solutions of from ½ to 10 per cent. have been used by the different authors. It often seems as if they retard the fatal result. In *Bright's disease* alkalies act beneficially by aiding in the removal of the œdema through their diuretic effect and possibly also by aiding in the solution or dislodgment of fibrinous exudates in the renal tubules.

They are indicated as expectorants in *bronchitis* or in other

conditions of the respiratory tract where tenacious mucus must be removed. They are used locally to cleanse various mucous membranes, as those of the nose and throat in catarrhal processes. On the skin in the form of baths they soften its superficial layers and stimulate its nutrition so that certain *skin diseases* are at times benefited by alkaline baths.

Magnesium Oxide is the most valuable agent for neutralizing the excess of hydrochloric acid in the stomach in cases of ulcer, erosions, pyloro-spasm and acid gastritis. It is also very valuable as a laxative in the dose of ½ to 2 teaspoonfuls mixed in ⅓ glass water before retiring at night.

MATERIA MEDICA.

Potassii Hydroxidum (U.S.P.), Potassa Caustica (B.P.), dry, white, translucent pencils or fused masses, odorless, or having a faint odor of lye and a very acrid and caustic taste. Exposed to the air, it rapidly absorbs carbon dioxide and moisture and deliquesces.

Liquor Potassii Hydroxidi (U.S.P.), Liquor Potassæ (B.P.), contains 5 per cent. potassium hydrate. **Dose:**—0.5 to 2.0 c.c. Br. (5–20 ♏). Average (U.S.P.), **1.0 c.c.**

Potassa Cum Calce (U.S.P.), grayish-white deliquescent powder, containing equal parts of potassium hydrate and calcium oxide.

Potassii Carbonas (U.S.P., B.P.), white, granular, odorless powder with a strong alkaline reaction and taste, deliquescent, very soluble in water, but insoluble in alcohol. **Dose:**—0.5 to 2.0 G. Br. (5–20 grains). Average (U.S.P.), **1.0 G.**

Potassii Bicarbonas (U.S.P., B.P.), colorless, odorless crystals with a slightly alkaline and saline taste and permanent in air. Soluble in 3.2 parts of water, almost insoluble in alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–40 grains). Average (U.S.P.), **2.0 G.**

Potassii Acetas (U.S.P., B.P.), white powder or crystalline mass, odorless, but having a saline taste. Very deliquescent. Very soluble in water, soluble in 1.9 parts of alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–40 grains). Average (U.S.P.), **2.0 G.**

Potassii Citras (U.S.P., B.P.), deliquescent, white crystals having a cooling saline taste. Very soluble in water, slightly soluble in alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–40 grains). Average (U.S.P.), **1.0 G.**

Potassii Citras Effervescens (U.S.P.), white, odorless powder containing 63 parts of citric acid, 90 of potassium bicarbonate, 47 of sugar. **Dose:**—0.5 to 4.0 G. Average (U.S.P.), **4.0 G.**

Potassii Oleas, or soft soap.

Sodii Hydroxidi (U.S.P.), Soda (B.P.), dry, white, translucent pencils or fused masses, odorless, having an acrid caustic taste.

Liquor Sodii Hydroxidi (U.S.P.), Liquor Sodæ (B.P.), contains 5 per cent. sodium hydrate. **Dose:**—0.5 to 2.0 c.c. Br. (5–20 ♏). Average (U.S.P.), **1.0 c.c.**

Sodii Carbonas (U.S.P., B.P.), colorless, odorless crystals, having a strong alkaline taste and reaction. Effloresces in the air. Very soluble in water, insoluble in alcohol and ether. **Dose:**—0.3 to 1.0 G. Br. (5–15 grains). Average (U.S.P.), **0.25 G.**

Sodii Bicarbonas (U.S.P., B.P.), white powder with a cooling, alkaline taste. Soluble in 11.3 parts of water, insoluble in alcohol and ether. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **1.0 G.**

Trochisci Sodii Bicarbonatis (U.S.P., B.P.) contains 0.2 G. sodium bicarbonate. **Dose:**—1 to 6 troches.

Sodii Boras (U.S.P.) or Borax, white crystalline powder, soluble in water. **Dose:**—Average (U.S.P.), **0.5 G.**

Sodii Acetas (U.S.P., B.P.), colorless, odorless, efflorescent crystals, having a cooling, saline taste, very soluble in water, soluble in 30 parts of alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **1.0 G.**

Sodii Oleas, or hard soap.

Calx (U.S.P., B.P.), hard, grayish-white masses which attract water and carbon dioxide and fall into a white odorless powder (slaked lime).

Liquor Calcis (U.S.P., B.P.) contains .17 per cent. of calcium hydrate. **Dose:**—5.0 to 30.0 c.c. Br. (1–4 ℥).

Calcii Carbonas Præcipitatus (U.S.P., B.P.), white, odorless, tasteless powder practically insoluble in water and alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **1.0 G.**

Creta Præparata (U.S.P., B.P.), a white, amorphous powder, odorless and tasteless, almost insoluble in water and alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **1.0.**

Pulvis Cretæ Compositus (U.S.P., B.P.) (compound chalk powder) contains 30 parts of chalk, 20 of acacia and 50 of sugar. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **2.0.**

Mistura Cretæ (U.S.P.) contains chalk powder and cinnamon water. **Dose:**—5.0 to 20.0 c.c. Average (U.S.P.), **16.0 c.c.**

Trochisci Cretæ (U.S.P.) contains .25 G. of chalk per troche.

Calcii Phosphas Præcipitatus (U.S.P.), Calcii Phosphas (B.P.), amorphous, odorless, tasteless powder, permanent in air. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **2.0.**

Syrupus Calcii Lactophosphatis (U.S.P., B.P.). **Dose:**—5.0 to 10.0 c.c. Average (U.S.P.), **8.0 c.c.**

Magnesii Oxidum Ponderosum (U.S.P.), Magnesia Ponderosa (B.P.), white powder without odor, but with an earthy taste, almost insoluble in water and alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **2.0 G.**

Magnesii Carbonas (U.S.P.), white powder, almost insoluble in water and alcohol. **Dose:**—0.5 to 4.0 G. Br. (5–60 grains). Average (U.S.P.), **3.0 G.**

Lithii Carbonas (U.S.P., B.P.), a white, alkaline powder, soluble in 80 parts of water, insoluble in alcohol. **Dose:**—0.2 to 0.5 G. Br. (3–10 grains). Average (U.S.P.), **0.5 G.**

Lithii Citras (U.S.P.), a white powder, soluble in 2 parts of water, insoluble in alcohol. **Dose:**—0.2 to 1.0 G. Average (U.S.P.), **0.5 G.**

Lithii Citras Effervescens (U.S.P.) contains about 7 per cent. lithium citrate. **Dose:**—0.5 to 4.0 G. Average (U.S.P.), **8.0 G.**

GROUP OF NEUTRAL SALTS.

The pharmacological action of neutral salts is dependent both upon their chemical and physical properties. The action, which depends upon the physical properties of salts being so characteristic of the latter, is surnamed **salt action.**

Some neutral salts pass easily through most animal membranes, others diffuse with difficulty. The former are rapidly absorbed by the intestinal mucous membrane, while the latter remain almost unabsorbed.

"SALT ACTION."

Salt action is thus called, because it is a physical action, characteristic of salts, yet it may be seen with cane-sugar.

This action may be briefly described as the change in proportion between certain solid elements as salts, and liquids as water, in some inert colloid, as in gelatine plates or in living tissues. This process depends upon diffusion and the tendency of two fluids containing varying proportions of salts to become of equal density. Thus, the water passes over to the more concentrated solution, while the salt flows in the opposite direction to the more dilute solution.

When no specific irritant qualities are possessed by salts, this salt action may alone be able to irritate body tissues, the intensity of the irritation varying, to a certain extent, with the difference of concentration of the salt solution in relation to that of body fluids. Solutions of equal concentration to blood serum are said to be *isotonic.* Solutions of greater concentration are said to be *hypertonic,* while those of lesser concentration are said to be *hypotonic.*

Both hypotonic and hypertonic solutions change the composition of protoplasm and irritate the same. On blood corpuscles, hypotonic solutions cause a diffusion of the hemoglobin out of the cells.

By varying its salt concentration, the entire living organism may be definitely affected in its metabolism.

Although a few years ago, almost all action of neutral salts was ascribed to their physical properties—*i. e.*, "salt action"; nowadays, new evidence has been brought forward to show special chemical action with nearly all salts, even with sodium chloride. The truth is that the action of neutral salts is dependent upon both salt action and specific ionic action. With some, the salt action is paramount, as with sodium chloride, while with others, as the bromides, the ionic action is most important.

ACTION DUE TO IONIC CONSTITUTION.

Although the physical "salt action" forms an important part of the action of some salts, yet a specific action, due to the ionic composition, exists in all. Sodium Chloride, which is such an important and copious constituent of all soft body tissues, has the least effect. In fact it is its absence or diminution which causes most important changes. Thus sodium and chlorin ions have very low toxic effects and it is only in very large doses that any such can be elicited.

The animal organism is protected against the toxic action of sodium, potassium, calcium and magnesium when introduced by mouth, by the fact that the simple compounds of these are absorbed more slowly than they are excreted. This process prevents the accumulation of a toxic amount after internal administration. The case is very different after intravenous administration, when the chloride salt of all these proves toxic, and as interestingly proved by Meltzer and Joseph the toxicity varies inversely with the amount of these present in the animal serum. The smaller the amount of the ion in the serum, the more toxic it is in the infusion. Thus sodium is least toxic. Next comes potassium which is half as toxic as calcium; while calcium is three times less toxic than magnesium. Below is a table extracted from the article by Meltzer and Joseph which is self-explanatory.

TABLE BY MELTZER AND JOSEPH

Substances	Existing in the Blood in Relative Concentration	Fatal in Relative Doses
Magnesium	1.00	1.00
Calcium	3.36	2.80
Potassium	7.81	4.26
Sodium	131.38	25.54

Other ions, as those of barium, iodin, and bromin, exert their specific effect even after internal administration. This is possible because the ratio between their absorption and excretion is such that an amount may accumulate in the blood sufficient to produce their specific pharmacological action.

GENERAL ACTION OF SALTS OF DIFFICULT ABSORPTION.

This class is chiefly represented by the sulphates and phosphates. Taken internally, they may produce nausea and vomiting both on account of their disagreeable bitter taste and because of their local action on the stomach.

As they are *difficultly absorbed*, but at the same time *readily excreted*, they are never present in the blood in sufficient quantities after internal administration to alter the **metabolism.** When applied to the **skin** they irritate it according to their concentration. They alter its nutrition and thus may influence different skin affections, although they are not absorbed except in the most superficial layers of the epidermis. Thus, by external application, they cannot pass into the blood, therefore do not influence the metabolism directly, although by their local irritant effect they may change the nutrition of the body in a reflex manner.

If sodium sulphate is injected subcutaneously or intravenously, it then exerts a marked effect upon the body fluids and the nutrition, and increases enormously the secretion of urine just as the members of the sodium chloride class.

GENERAL ACTION OF SALTS OF EASY ABSORPTION.

Whenever solutions of **SODIUM CHLORIDE** or other easily absorbable salts of this division as other chlorides, iodides, bromides, etc., come in contact with tissues containing less salts, they draw water from them. They tend to pass into the tissues or on the other side of the membranes and when their concentration is equalized on both sides, their action ceases. They are more rapidly absorbed by the stomach in concentrated, but by the intestines in diluted solutions.

Locally applied to the **skin,** they cause irritation. This irritant effect is followed by a slight local anæsthetic action, especially observed with bodies containing potassium or bromide ions. They also act as mild antiseptics in sufficient concentration. After internal administration, the irritant action is well marked on the mouth, œsophagus and stomach so that nausea and vomiting occur after large doses. These, long continued, may even produce catarrh of the stomach.

Since they are rapidly absorbed from the upper part of the **small intestines,** they exert no direct influence on the lower portion nor upon the large bowel, and therefore cause but an insignificant cathartic action compared with the members of the sodium sulphate group.

On the other hand, they produce a marked influence on metabolism, and they increase markedly the secretion of the kidneys and also that of the bronchial mucous membrane which they make more fluid and less tenacious.

These salts increase the **metabolism** by augmenting the interchange of fluids in the body, thus exciting the tissues to greater activity. As soon as they are absorbed into the blood, the latter having greater osmotic pressure draws water from the lymphatics and tissues; but the salts also pass into both these and are excreted by the kidneys so that the osmotic pressure of the blood diminishes again. Fluids pass from the blood to the lymph and tissues, but as more of the salts are absorbed from the intestines,

the blood again acquires a greater osmotic pressure and the currents change and thus the circle continues.

Increased metabolism may result after the external application of salts in the form of baths. In this instance the effect is only reflex by the local irritation, for they are *not absorbed by unbroken skin.*

The urine voided by an animal is the sum of the fluid and various solid constituents which have diffused through the glomeruli, minus that portion which has been reabsorbed by the convoluted tubules. The salts act as **diuretics,** probably both by increasing the bulk of the blood and therefore the quantity circulating through the kidneys, and by decreasing the reabsorption of fluids by the convoluted tubules. Some, such as chlorates and nitrites, seem to exert a direct irritant action upon the kidney.

The salts of this division act as expectorants by virtue of their local irritant action after excretion on the **bronchial mucous membrane** and by their power of softening mucus. This solvent action on mucus can also be observed in the stomach when it contains an excessive amount as in catarrh.

These salts, as well as those of the sodium sulphate group, often cause an increased thirst on account of their affinity for water and because by their action they tend to decrease the water of the body.

INTESTINAL ACTION OF SALTS.

The easiest way to present the mode of action of the neutral salts on the *intestines* is to quote from the author's experimental conclusions.

The neutral salts can be divided into four classes: **first,** those which do not exert a marked stimulant action on the mucous membrane of the intestines leading to increased peristalsis, as *sodium chloride;* **second,** those which exert a marked stimulant action on the mucous membrane of the intestines leading to increased peristalsis, as sodium phosphate and *sodium sulphate;* **third,** those which, although stimulating the mucous membrane and leading to peristalsis, depress the neuro-muscular elements

when applied to them, such as *magnesium sulphate;* **fourth,** those which exert a special stimulant action on the neuro-muscular elements of the intestines, like physostigmine and ergot. These are best represented by *barium chloride.* It is difficult to draw a sharp line of distinction between class I and class II, because there are a number of salts which may produce a certain amount of peristalsis but not powerful enough to cause rapid onward movement of the intestinal contents, which would stand between the two classes.

The three salts, magnesium sulphate, sodium sulphate and sodium phosphate, **act very differently when applied to the mucous membrane or to the serous surface of the intestines, in fact, the action is opposite.** It is known that these salts are absorbed with difficulty from the mucous membrane of the intestines, while infinitely more easily from the subcutaneous or serous channels. Therefore, it is fair to suppose that the action after the application to the serous surface of an extirpated intestine separated from the central nervous system represents the effect after absorption upon the neuro-muscular elements of the intestines. On the contrary, the results obtained after application to the mucous membrane can, in view of these experiments, be considered rather as a local effect, something after the manner of the skin irritants. The question then arises whether this local irritant effect is dependent upon the power of the salts to draw water from the cells of the mucous membrane and thus to stimulate or irritate these, or whether the stimulation depends upon the chemical constitution of the salt. The author believes that the second condition is paramount, because the amount of stimulation only depends to a certain point upon the concentration of the salt solution and furthermore, these, which are all three "purgative salts," show much more stimulant effect than sodium chloride (not a purgative salt) in hypertonic solutions.

It would seem as if **purgation by these salts was dependent on a specific irritation of the mucous membrane responded to by a reflex increased motor activity.** Catharsis by drugs is certainly not wholly dependent upon general intensity of the irritation but rather upon the specificness of the stimulation.

Magnesium in most of its common combinations is well known to depress the motor activity of the neuro-muscular elements of the intestines, yet the insoluble magnesium oxide in such doses as ½ to 1 teaspoonful (personal observations on different human beings) where exclusive "salt action" is not probable, has undoubted purgative action, although very little irritant effect. It probably forms a chloride in the stomach and salts of fatty acids in the intestines which however, are probably not great irritants, for no matter how large the dose (8–10 teaspoonfuls), no gastro-intestinal inflammation has been observed. (Author's observation.) It thus seems plausible that some magnesium salts have a special stimulant action on the mucosa leading to a reflex resulting in purgation.

That the change in osmotic pressure brought about by those salts taken in large quantities may be partially concerned in the stimulation, cannot be denied, but from my experiments, I certainly could not see the situation in the light of all the other authors with the osmotic pressure theory, that the drawing of fluids from the vessels into the intestines or the retaining of the fluids which are already in the lumen is the chief cause of catharsis; because in my personal experiments increased effective movements were obtained before there had been time for the passage of much fluid from the outer into the inner portion of the gut. Furthermore, in series No. 1 by comparing the quantity of fluid which entered and left the intestine there was never a large surplus, not more than 2–3 c.c. in 30–40 c.c., which had passed the intestine. The experiments of Merckx support the author's view that the hygroscopic action of salts is not essential in purgation. He examined the concentration of the intestinal contents at different levels after saline purgatives, and found that the concentration in cathartic salts was greater at the lower than at the upper fistula. Thus he showed that in living animals purgative salts do not steadily increase the watery contents of the intestine in their passage downward.

Concerning the influence of salts placed in the nutritive medium in contact with the serous surface of the intestines, the following

may be said. As might naturally be expected, any substance changing to an appreciable degree, qualitatively or quantitatively, the normal nutritive fluid will ultimately deteriorate the very sensitive intestine. The difference of action is more marked with some substances than with others, as for instance, magnesium sulphate has a far more depressive effect in the nutritive medium than sodium sulphate or sodium phosphate. If sodium sulphate or sodium phosphate are injected into the blood of living animals they may exert little or no paralyzing effect upon the intestine because being so diluted in the circulation, it is difficult to inject enough to sufficiently change the composition of the nutritive medium, the blood. With magnesium sulphate, as has been shown by Meltzer and Auer and others, small amounts injected into the blood will paralyze the intestine because this salt probably has specific attractions for the neuro-muscular mechanism of the intestine, as in the case of atropine. Only the purgative effect and not the paralyzing action of magnesium sulphate is usually observed when given by mouth to man and other animals because not enough enters the circulation to exert the paralyzing effect upon the neuro-muscular element of the intestine, while a sufficient quantity is in contact with the mucous membrane towards which it exerts a stimulant action, causing reflex increase of peristalsis (by reflex is meant local reflex in the intestinal wall). Thus the discrepancy of opinions between the authors who observed the purgative action of magnesium sulphate and those who observed a paralyzing effect on the intestine is easily explained.

An apparent exception to the fact that a change in the normal nutritive medium of the isolated intestine injures the latter and depresses it, is the fact that barium chloride, ergot and physostigmine, etc., increase the force of contraction when applied in this way. With these drugs the strong specific stimulation to the neuro-muscular element of the intestine masks the effects incident to the change in the medium, and besides their action occurs in such minute doses that a very little quantitative change from the normal occurs in the medium.

Concerning the old disputed question as to whether or not salts may act as a purgative when injected intravenously or subcutaneously, as would appear in the author's plan, depends enormously on the individuality of the salt. Thus those of the fourth class, as barium chloride, produces marked catharsis by intravenous or subcutaneous injections (catharsis by subcutaneous or intravenous injections of barium chloride in rabbits and other animals is admitted by every one who has ever tried it). The third class, typically represented by magnesium sulphate, would produce the contrary effect and paralyze the intestine by intravenous injections (discrepancy of opinion in this case probably depends on faulty technique or experimental inaccuracies). Those of the first and second class which have little or no action on the neuro-muscular elements would produce little or no effect by subcutaneous or intravenous injections.

From all these observations, the author believes that peristalsis is the most important feature in purgation, because no matter how much water is present in the intestine if the neuromuscular element of the latter is depressed, onward movement does not well occur. Yet, one should distinguish between superficial peristalsis accomplishing but little, and deep effective peristaltic activity, pushing and squeezing forward the contents, and it is probably in this sense that the author differs from Auer, for when this latter experimenter obtained increased peristalsis from the subcutaneous administration of some salts but no purgation, he concluded that peristalsis alone does not necessarily cause purgation.

SPECIAL ACTION DUE TO IONIC CONSTITUTION.

Sodium chloride or "common salt" is a necessary component of the organism. If an animal is fed on food which contains no sodium chloride he dies in a short time. Meats contain sodium chloride, but vegetable food contains very little, so that herbivora always seek for salt. Vegetable food not only does not furnish sufficient sodium chloride to the organism, but takes it away from the reserved supply in the following manner. The potassium phosphate present in large quantities in vegetable food re-

acts in the blood with the sodium chloride to form potassium chloride and sodium phosphate. These two salts are both rapidly excreted and thus the sodium chloride is lost. The loss could not take place without this reaction because the body retains sodium chloride tenaciously when only normal quantities are present.

Sodium chloride is one of the salts most important to life, yet the others normally present in the body have also essential functions. When the former is injected intravenously it produces poisonous symptoms only when immense doses are used, so we deduce that both the sodium and the chlorine ions have very little tonic action. However, it is not so with the dissociated ions of potassium, calcium, bromine and iodine, etc., present in other neutral salts.

POTASSIUM SALTS may produce death in doses of 7 to 8 mg. per kilo body weight when injected into the blood circulation. *They depress the central nervous and muscular systems and heart,* causing a slowing of the pulse and a sinking of the blood pressure. They produce death by cardiac paralysis.

These symptoms can all be elicited both by intravenous and subcutaneous administration, but not when taken by the mouth, because then their excretion keeps pace with their absorption and never enough is present in the blood at one time. Locally they paralyze peripheral nerves. They are more irritant locally than sodium salts and also have a greater diuretic action.

CALCIUM forms many insoluble and difficultly diffusible salts, but even the soluble ones are absorbed with great difficulty. After absorption it is excreted in the urine of herbivora, but in man mainly in the large intestines.

Although a normal constituent of the highly organized body, calcium produces poisonous symptoms when injected into the blood in sufficient quantities. At first, it *stimulates and strengthens the heart, but later depresses it.* It also depresses the central nervous system.

The lack of sufficient calcium in food, or *lime starvation,* is capable of producing marked changes, especially in the growing organism. As it is one of the main constituents of bone, an in-

sufficient amount in food leads to softening of bones and conditions akin to rickets and osteomalacia.

MAGNESIUM salts have only of late attracted interest concerning their internal action, although their purgative one has been studied and used practically for many years.

As a rule, they do not produce constitutional action after internal administration in man and many warm-blooded animals. Cannon discovered years ago that magnesium sulphate caused constitutional poisoning in cats after oral administration. Others have lately reported cases of poisoning in human beings after a purgative dose of magnesium sulphate. The discovery of this untoward action was rather startling, as epsom salt had been considered for scores of years as a harmless purgative. Such poisoning effects in man are, however, very rare because magnesium is as a rule excreted much faster than it is absorbed.

Given intravenously or subcutaneously, magnesium salts are very toxic, much more so even than those of calcium and potassium.

Their action consists of a paralysis of the motor end plates (curare-like), of the muscles of the central nervous system and heart. Death results from **respiratory failure** which is *due to the combined paralysis of the respiratory center and of the respiratory muscles*. Meltzer and Joseph were able to show a very interesting antagonistic action of physostigmine toward magnesia.

When applied to nerve trunks, injected into the spinal canal or over the cerebrum, magnesium salts exert a *local anesthetic action* just like cocain.

LITHIUM, STRONTIUM, RUBIDIUM and **CÆSIUM** salts have an action similar to that of potassium salts.

BARIUM salts produce convulsions in frogs similar to those caused by picrotoxin. In these animals, they stimulate and then depress the **heart** just as the members of the digitalis group.

In the warm-blooded, the **symptoms** after intravenous or subcutaneous injection consist of vomiting, diarrhœa, sometimes light convulsions and death due to paralysis of the heart. There is at the beginning of the poisoning a characteristic *rise*

of blood pressure which is due both to stimulation of the vasomotor centre and to direct action upon the vessel walls.

Cases of **poisoning in man** exhibit chiefly great general weakness and motor paralysis of the limbs and of the sphincters of the bladder and anus. Deglutition is also impaired. The fatal dose of barium salts for rabbits, cats and dogs is 0.1–0.3 G. per kilo by subcutaneous injection.

AMMONIUM compounds produce an *intense stimulation of the central nervous system* when injected subcutaneously or into the blood. This was described in detail in a previous chapter.

The **SULPHATE** ions in neutral salts have in common with the chlorine ions, weak action.

SULPHITES, through their dissociated ions, produce chiefly a *paralysis of the central nervous system and heart* after subcutaneous or intravenous injection. The fatal dose for rabbits is 0.6 G. per kilo by subcutaneous injection.

The **ORTHO-PHOSPHATE** ions produce little action, even after subcutaneous injection; but on the other hand, the *pyro-* and *meta-phosphate* produce fatty degeneration analogous to phosphorus, but only after subcutaneous or intravenous administration.

CHLORATES are easily absorbed from the intestinal tract, even in quantities sufficient to produce poisonous symptoms. Besides their local irritant action, which is great, they possess a special action on **red blood corpuscles.** They break up the latter and transform the hæmoglobin to methæmoglobin. They produce cyanosis, dyspnœa, feeble heart, headache, muscular weakness and death due to asphyxia. After internal administration they cause severe *gastro-intestinal irritation.*

Given in smaller doses over a period of time they produce inflammation of the **kidneys** which results in uremia and death. This is due both to the local irritant action of the chlorates and of the free hæmoglobin and methæmoglobin during their excretion by these organs.

They are **excreted** almost in toto by the urine; yet some believe that a small quantity passes into the saliva.

NITRATES have a severe irritant action; in fact, greater than can be accounted for by their salt action.

In large quantities, they are *destroyed in the body*, probably reduced to ammonia. They produce a marked stimulation of the kidney which at first leads to an increased secretion, but later to inflammation and anuresis.

FLUORIDES at first stimulate then depress the **medulla,** so that they cause increased respiration and circulation and also convulsions, succeeded by general paralysis and death due to stoppage of respiration, while the heart and skeletal muscles remain unaffected throughout the poisoning. The fatal dose given subcutaneously to animals is 0.10–0.15 G. per kilo body weight.

BORATES and boric acid (the latter is so weak an acid that its action is the same as that of its salts), produce great *hyperemia of the intestinal mucosa* even after subcutaneous injection. The Peyer's patches are much swollen and there may be an exudation of bloody fluid in the gastro-intestinal tract after internal administration.

The **symptoms** consist of nausea, vomiting, diarrhœa, and collapse which is possibly due to the dilatation of the vessels of the splanchnic area just as with arsenic.

After long use of boric acid preparation the **kidneys** may become irritated and secrete albuminous urine and the **skin** frequently exhibits eruptions. With large doses given over a period of time, they seriously disturb the proteid **metabolism,** decreasing the absorption and increasing the combustion. They are very rapidly absorbed and **excreted** by the urine within thirty-six hours after ingestion.

BROMIDES possess a very characteristic action not approached by that of any of the other halogen ions.

The most striking effect is upon the **central nervous system,** especially on those parts of the cord connected with reflex action and those parts of the brain concerned with sensation and intellect. When given to the average human being in moderate medicinal doses (1 gramme or 15 grains three times daily), they

produce few symptoms, except a sensation of relaxation and well-being. If there have been sleeplessness and nervousness, these states are corrected and besides a long night's sleep, a tendency to somnolence may occur during the day.

When a large dose is given for a period of time, much more intense symptoms from the central nervous system may arise. These consist, sometimes of extreme somnolence; sometimes of dulling of the intellect, with defect of memory, difficulty of expression and rarely of depression of spirits and melancholia. The gait is rarely affected, although with enormous doses it may become somewhat unsteady.

Like other salts of this group, bromides have a well-marked, **local irritant action,** which may be seen at the place of administration, and also at the place of excretion.

The **stomach** is particularly prone to irritation by the bromides when these are administered without sufficient food or alkalies, because, besides the irritant action of the salts themselves, the even more irritant hydrobromic acid is formed in the presence of free hydrochloric acid. Many physicians exclude bromides from their materia medica because of the nausea, occasional vomiting and other dyspeptic symptoms occurring after the improper use of these salts. This irritation can be easily overcome by administering bromide, always in the presence of an excess of alkalies, and immediately after a full meal, which contained no acids. Under these circumstances, the author has never seen a case of gastric irritation, even in dyspeptics.

Bromides are **excreted** by nearly all the excretory organs of the body, but chiefly by the urine. No inflammatory symptoms have ever been found in the kidneys after these drugs, yet, not infrequently, the **diuresis** is greatly increased, and occasionally, a burning sensation may be felt in the urethra.

A certain amount of bromides are excreted by the **skin** and probably in consequence, a considerable percentage of people with irritable skins exhibit a skin eruption after the administration of large medicinal doses of bromides. These eruptions usually take the form of acne papules or pustules and also of red

blotches. Other kinds of skin lesions may occasionally be seen after their administration.

Unlike the iodides, bromides seldom irritate the respiratory tract, yet, occasionally, a little bronchial, pharyngeal or nasal irritation, with increased secretion may be seen, after bromides. Through their excretion into the mouth, they may produce a disagreeable metallic taste; also an offensive breath.

The **heart** is never affected by these drugs, when administered by the mouth. The term **bromism** has been applied when any of the untoward effects of bromides occur. All of these disappear rapidly when the drug is withdrawn. It is said that the taking of very large amounts of bromides for a long time, may induce a certain cachexia, which makes patients more likely to infectious diseases.

IODIDES, unlike bromides, do not produce a well-marked pharmacological action on the central nervous system, but they have much greater action on the general **metabolism.** When given in large doses for a long period of time, they may lead to extreme emaciation and **cachexia.** Iodides also have a specific effect in *stimulating the thyroid secretion*, and in diseases with an increase of this secretion, as in exophthalmic goitre, they may cause alarming symptoms, such as excessive palpitation, great nervousness and sleeplessness and tremors.

Like bromides, only much more intensely, iodides produce marked **irritation** at the place of absorption and place of excretion. With iodides, the respiratory tract suffers most; and very distressing coryza, running of the eyes, pharyngitis, laryngitis and bronchitis may occur after medicinal doses. Even œdema of the larynx, necessitating tracheotomy, has occasionally been observed in man.

Skin eruptions following the use of iodides are also exceedingly common and may take the form of any of the skin lesions. These result in sensitive skins from the excretion of some of the iodides by the skin.

Although **excreted** in large part by the urine, iodides do not

seem to produce inflammation of the kidney, but they may cause irritation of the bladder, urethra and vagina.

The **stomach,** particularly after oral administration, is especially prone to irritation. Loss of appetite, nausea, vomiting and other dyspeptic symptoms are the frequent sequence of the administration of iodides. As in the case of bromides, these can be, to a certain extent, overcome by giving the iodides with an alkali, well-diluted with milk, after full meals.

The most important, yet, unexplained action of iodides in practical medicine, consists in their marvelous curative action in the tertiary stages of syphilis. In this disease, they may cause the disappearance in a few days to a few weeks of large gummata and also of tertiary skin affections.

Iodism is a term applied to the untoward effects of iodides.

SUMMARY OF GROUP ACTION.—*Salt action, producing with the easily diffusible members changes in the general metabolism, a solution of the mucus in the bronchi and stomach, and an increase in the secretion of urine. While with the more difficultly absorbed members, having specific stimulant properties on the mucosa of the intestines causing augmentation of peristalsis resulting in purgation, also special effects due to the ionic constitution of the salts observed on the central nervous system, heart and musculature after subcutaneous or intravenous administration with all salts and even after internal administration with some of them.*

THERAPEUTIC APPLICATION.—Some of the neutral salts, including **sodium chloride, sodium sulphate** and **magnesium sulphate,** are used in the treatment of *stomach catarrhs*. In these conditions, they probably exert their beneficial influence firstly by dissolving the mucus which covers the lining of the stomach and interferes with the secretion and admixture of the gastric juice with the food; secondly, through their local irritant action by increasing the peristalsis of the atonic stomach, thus relieving retention.

Sodium chloride is also of value in increasing the peristalsis of the *small intestines* and dissolving mucus which may be there, but as it is rapidly absorbed it does not influence the large bowel.

Since the members of the sodium sulphate group, including **sodium sulphate, sodium phosphate** and **magnesium sulphate** act by increasing the peristalsis of the intestinal tract, they are used as *purgatives*. In small doses, they are employed to relieve *constipation;* in large ones to produce profuse watery evacuations, and thus to rid the intestinal tract of obnoxious material, either poisons from the outside or irritative products of fermentation. During their purgative action they draw the blood to the intestines and so may relieve the congestion in other organs such as the brain, liver, kidney, etc. By decreasing the watery constituents of the blood they may help the *absorption of œdemas and effusions*.

Since the members of the **sodium chloride group** are absorbed and excreted by the kidneys, they may be used as *diuretics* and because of their excretion in the bronchi, as expectorants. As a diuretic, sodium chloride has been used especially in the form of mineral waters. To increase the bronchial secretion and to render the *bronchial mucus less tenacious*, potassium iodide is especially useful.

All the salts of the sodium chloride type can be used to increase the general metabolism. Sodium chloride in the form of mineral waters is much employed for this purpose, but the most active members of the group on the nutrition are the **iodides.** They have been used to *increase the metabolism* in practically all conditions where it is believed to be faulty, as *gout* and *rheumatism*, but they have been found especially valuable in the tertiary and secondary stages of *syphilis*. They are given with marvelous results to remove syphilitic gummata. They are also employed with considerable success for *simple goitre;* and in a number of cases, they have been found useful to remove certain *lympho-sarcomatous glands*. This action of dissolving tumors of different natures cannot be explained alone by the increased metabolism due to their salt action. Possibly part of this effect is due to the formation of an easily soluble and excreted iodine compound between the iodine and the proteids of the tumor.

Potassium iodide has also been used with some degree of success in the treatment of *arterio-sclerosis* and *aneurysm*. In the cases where benefit occurred it is possible that this was due to the fall of blood pressure occasioned by the potassium element, and also to changes in the metabolism of the arterial walls.

Bromides are used especially to decrease the functional activity of the central nervous system as in cases of *nervousness*, *sleeplessness* and *epilepsy*. Paradoxical as it may seem, since bromides have an irritant action upon the stomach, yet, if administered in the proper manner, they are often very valuable in *gastric neuroses*, *acid gastritis and gastrospasm*. In the last mentioned disease, they are found to diminish both the intensity and the frequency of the attacks. If epilepsy is due to irritation of the cortex, this action may be explained by the influence of the bromides in depressing the motor areas of the brain.

Potassium chlorate is used as a mouth wash and *gargle* in inflammation of the mouth and throat and also as an instillation in inflammation of the *sigmoid* and *rectum*. There, it probably acts only through its salt action as a mild antiseptic and by removing excessive mucus.

Potassium nitrate was formerly employed considerably, but now only seldom as a *diuretic*.

Calcium phosphate and other phosphates were used in various bone diseases to replace the normal bone constituents, but since they are so poorly absorbed, they exert no such influence. In some osseous diseases even more calcium and phosphates may be excreted by the feces and urine than have been given in the food.

MATERIA MEDICA.

Non-purgative Division.

Sodii Chloridum (U.S.P., B.P.), or common salt, white crystals, odorless, with a salty taste. Very soluble in water, almost insoluble in alcohol. **Dose:**—0.5 to 4.0 G. Br. (10–60 grains.) Average (U.S.P.), **16.0 G.**

Ammonii Chloridum (U.S.P., B.P.), white crystals, very soluble in water, insoluble in alcohol. It has a cooling, saline taste. **Dose:**—0.5 to 2.0 G. Br. (10–30 grains.) Average (U.S.P.), **0.5 G.**

Potassii Chloridum, white crystalline body, very soluble in water, and practically insoluble in alcohol. **Dose:**—0.5 to 2.0 G.

Lithii Chloridum, white crystals, very deliquescent, soluble in water. **Dose:**—0.5 to 2.0 G.

Sodii Bromidum (U.S.P., B.P.), white crystals having a saline, bitter taste. Very soluble in water. Soluble in 13 parts of alcohol. **Dose:**—0.5–2.0 G. Br. (10–60 grains.) Average (U.S.P.), **1.0 G.**

Potassii Bromidum (U.S.P., B.P.), white crystals easily soluble in water but only in 180 parts of alcohol, disagreeable, salty bitter taste. **Dose:**—0.5 to 2.0 G. Br. (10–60 grains). Average (U.S.P.), **1.0 G.**

Ammonii Bromidum (U.S.P., B.P.), colorless crystals, with a pungent, saline taste. Very soluble in water, soluble in 30 parts of alcohol. **Dose:**—0.5 to 4.0 G. Br. (10–60 grains). Average (U.S.P.), **1.0 G.**

Lithii Bromidum (U.S.P., B.P.), is a white, granular salt, bitter taste, very deliquescent, very soluble in water and alcohol. **Dose:**—0.5 to 2.0 G. Br. (10 to 20 grains). Average (U.S.P.), **1.0 G.**

Calcii Bromidum (U.S.P.), white, granular, having a sharp saline taste, and very deliquescent. Very soluble in water and alcohol. **Dose:**—0.5 to 2.0 G. Br. (10 to 20 grains). Average (U.S.P.), **1.0 G.**

Strontii Bromidum (U.S.P.), colorless, crystalline body having a bitter, saline taste, very deliquescent, very soluble in water and alcohol. **Dose:**—0.5 to 2.0 G. Average (U.S.P.), **1.0 G.**

Sodii Iodidum (U.S.P., B.P.), colorless crystals, having a saline, bitter taste, very soluble in water, soluble in 3 parts of alcohol. **Dose:**—0.5 to 4.0 G. Br. (10 to 60 grains). Average (U.S.P.), **0.5 G.**

Ammonii Iodidum (U.S.P.), colorless crystals, sharp saline taste, very deliquescent, very soluble in water, soluble in 9 parts of alcohol. **Dose:**—0.5 to 4.0 G. Average (U.S.P.), **0.2 G.**

Potassii Iodidum (U.S.P., B.P.), colorless crystals, with a faint, iodine-like odor and a pungent, saline, bitter taste. Very soluble in water, soluble in 18 parts of alcohol, 2.5 parts of glycerine. **Dose:**—0.5 to 4.0 G. Br. (10 to 60 grains). Average (U.S.P.), **0.5 G.**

Unguentum Potassii Iodidi (U.S.P.), contains 10 per cent. potassium iodide.

Potassii Nitras (U.S.P., B.P.), or saltpeter, colorless, odorless crystals, having a cooling, saline taste, very soluble in water, very sparingly soluble in alcohol. **Dose:**—0.25 to 1.0 G. Br. (5 to 15 grains). Average (U.S.P.), **0.5 G.**

Charta Potassii Nitratis consists of paper dipped in 20 per cent. solution of potassium nitrate.

Sodii Nitras (U.S.P.), (Chili saltpeter), colorless transparent crystals having a cooling, saline, bitter taste, deliquescent in air, very soluble in water, soluble in 100 parts of alcohol. **Dose:**—0.3 to 2.0 G. Br. (5 to 15 grains). Average (U.S.P.), **1.0 G.**

Potassii Chloras (U.S.P., B.P.), white crystal, saline, bitter taste, soluble in 20 parts of water. **Dose:**—0.1 to 0.5 G. Br. (2 to 5 grains). Average (U.S.P.), **0.25 G.**

Purgative Division.

Sodii Sulphas (U.S.P., B.P.), or Glauber's salt, large, colorless crystals, having an intensely bitter, saline taste, efflorescent in the air, very soluble in water, insoluble in alcohol. **Dose:**—10.0 to 30.0 G. Br. (½ to 1 ℥). Average (U.S.P.), **16.0 G.**

Potassii Sulphas (U.S.P., B.P.), colorless crystals, with a bitter saline taste, soluble in 9.5 parts of water, insoluble in alcohol. **Dose:**—5.0 to 15.0 G. Br. (2 to 4 ʒ). Average (U.S.P.), **2.0 G.**

Magnesii Sulphas (U.S.P., B.P.), Epsom salts, colorless crystals, with intensely bitter taste. Very soluble in water, insoluble in alcohol. **Dose:**—10.0 to 30.0 G. Br. (½ to 1 ʒ). Average (U.S.P.), **16.0 G.**

Sodii Phosphas (U.S.P., B.P.), colorless crystals, with a cooling, slightly saline taste, efflorescent in the air, soluble in 5 parts of water. **Dose:**—10.0 to 30.0 G. Br. (½ to 1 ʒ). Average (U.S.P.), **2.0 G.**

Potassii Bitartras (U.S.P.), Potassii Tartras Acidus (B.P.), or cream of tartar, colorless crystals, having a pleasant, acidulous taste, soluble in 201 parts of water, difficultly soluble in alcohol. **Dose:**—5.0 to 15.0 G. Br. (2 to 4 ʒ). Average (U.S.P.), **2. G.**

Potassii et Sodii Tartras (U.S.P.), Soda Tartarata (B.P.), or Rochelle salts, colorless crystals with a cooling saline taste, effloresces in the air. Easily soluble in water. **Dose:**—10.0 to 30.0 G. Br. (½ to 1 ʒ). Average (U.S.P.), **8.0 G.**

Pulvis Effervescens Compositus (U.S.P.), Pulvis Sodæ Tartaratæ Effervescens (B.P.) or Seidlitz powder, composed of Rochelle salt, sodium bicarbonate and tartaric acid. **Dose:**—Average (U.S.P.) one set of two powders.

Magnesii Sulphas Effervescens (U.S.P.), white, coarsely granular salt, with a mildly acidulous, refreshing taste. Deliquescent, easily soluble in water, almost insoluble in alcohol. **Dose:**—10.0 to 30.0 G. Average (U.S.P.), **16.0 G.**

Liquor Magnesii Citratis (U.S.P.), effervescent liquid, made by mixing magnesium carbonate, potassium bicarbonate and citric acid, corking and wiring immediately. **Dose:**—50.0 to 250.0 c.c. Average (U.S.P.), **360.0 c.c.**

GROUP OF PHOSPHORUS.

YELLOW PHOSPHORUS is the active form, for its allotropic modification or the red variety is inert, on account of the absolute insolubility of the latter in body fluids.

The yellow phosphorus itself is slowly **absorbed** on account of its difficult solubility, but there is an agent in the intestinal tract, bile, which greatly facilitates its solution and absorption. It probably enters the circulation in small quantities in the form of vapors, but only to a small extent as it is so little volatile at the temperature of the body.

On account of its slowness of absorption, **poisonous symptoms** may not appear for hours or even for a day after its ingestion. These consist first of a burning sensation in the œsophagus, stomach and abdomen, followed by persistent nausea, sometimes bloody vomiting with garlicky odor and diarrhœa. They are

followed in a few days by symptoms of great weakness, jaundice, distress and pain in the region of the stomach and liver, at first an increase, then a decrease in the secretion of urine, collapse and death. The pulse is weak throughout the poisoning and there may be also hemorrhages from the nose, uterus and subcutaneous tissues. The liver is usually felt much enlarged. Delirium and convulsions often precede the fatal ending in coma.

The gastro-intestinal symptoms are due to protoplasmic changes of the cells of this tract, beginning with cloudy swelling, then resulting in **fatty degeneration.** The ecchymoses and hemorrhages are due to degeneration of the vessel walls. The pain over the liver, the jaundice, the great diminution of urea in the urine, the appearance of leucin, tyrosin and large quantities of ammonia and lactic acid in this secretion are all due to interference with the functions of the **liver** on account of its destruction by fatty degeneration. It is said that the autolytic processes of the liver are increased and that these abnormal constituents in the urine are due to self-digestion of this organ. It is probable, however, that it is not the autolytic activity which is increased but the resistance of the cells against it which is decreased. The preliminary increase in the urine is due to the augmentation of urinary products, but the succeeding interference with this secretion is due to fatty degeneration of the **kidneys.** This widespread fatty degeneration even attacks the vessel walls and the fibres of the **skeletal muscles** and **heart.**

With this poison, the lower forms of organisms and ferments seem to remain unaffected, for **bacteria** are not killed or hindered in their activity. Peptic and pancreatic digestions and autolysis of organs go on just as well in the presence of phosphorus.

When death takes place after a few days, it is due to the general destruction of the various organs and the consequent great interference with **metabolism.** When it occurs early in the first hours of the poisoning, it is then due to direct paralysis of the heart muscles.

Phosphorus exerts little, if any direct effect upon the **central**

nervous system, neither does it affect the irritability of nerve muscle preparations.

Given in moderately small doses over a long period of time, phosphorus produces besides general cachexia and fatty degeneration of the different organs, a characteristic **connective-tissue formation** which may lead to cirrhosis of the stomach, liver or kidneys.

Administered in minute doses for a long time to young animals, it increases the cancellous structure of **bones,** converts cartilage and soft bone into hard bone. This osseous formation, as well as that of connective tissue, is probably due, at least in part, to a special stimulant action of phosphorus upon the cells. When its fumes are inhaled over a period of time, as by workers in match factories, besides cachexia, gastro-intestinal disturbance, anæmia and slight jaundice, marked evidences of its special action on bones may be seen. These, which are only observed when there are carious teeth, consist of necrosis of the jaw, leading to pus formation and throwing off of sequestra which, however, may heal perfectly with the formation of new bone.

In small doses in man, phosphorus has been found to increase the number of **red blood corpuscles,** due to a stimulation of the bone marrow, but in poisonous quantities it destroys red blood globules in most animals. It circulates through the blood, acts in the body as such, and is not transformed into phosphuretted hydrogen. It is **excreted** partly as such by the lungs, partly as a proteid compound and to only a small extent as phosphates by the urine.

Since phosphates are non-poisonous in the intestinal tract, various oxidizing agents are given as **antidotes** in phosphorus poisoning to oxidize the latter to phosphates. Some of these are potassium permanganate, hydrogen peroxide and turpentine; although these remedies are not as a rule very successful. Copper sulphate is also used because it produces an insoluble compound, but as this is again readily decomposed, it should be rapidly removed by emesis or purgation.

PHOSPHURETTED HYDROGEN or PH_3, is a colorless gas with the odor of garlic, which was formerly described as having the same action as phosphorus: in fact, some authorities believed that the latter acted in the body only after transformation into this gas.

Phosphuretted hydrogen does not have the identical action of phosphorus, although it is exceedingly toxic and produces death quickly in doses of 0.002 G. in rabbits. Its action is chiefly on the **central nervous system, heart** and **gastro-intestinal tract.** After a stage of vomiting and diarrhœa it kills by paralysis of respiration and circulation.

SUMMARY OF GROUP ACTION.—*Absorption difficult, but may be aided by bile. When large quantities absorbed, rapid death due to paralysis of the heart. In slow poisoning, extensive fatty degeneration of all parenchymatous organs, including liver, kidney, heart, skeletal muscles and arterial walls. At first vomiting and diarrhœa which becomes bloody. Urine diminished and contains amido acids, ammonia and but little or no urea. Delirium and convulsions precede death in coma.*

THERAPEUTIC APPLICATION.—Phosphorus has been used in various nervous affections and anæmia. Its chief field of application is to harden bone in diseases attended by a softening of these organs as *rickets* and *osteomalacia*. *Caries* and *ununited fractures* are sometimes treated by the administration of phosphorus internally.

Instead of phosphorus itself, various compounds of this element are used in its place for a tonic effect. These include *hypophosphites*, *glycerophosphates* and a derivative of the latter, *lecithin*, a normal constituent of the brain. These have been used on the theory that many debilitated conditions are due to a decrease of phosphorus in the body and that these compounds are eminently suited to replace this waste. No definite pharmacological action nor therapeutic results have ever been proved to follow the use of these substances.

MATERIA MEDICA.

Phosphorus (U.S.P., B.P.), translucent, colorless, or slightly yellowish waxy mass which emits fumes with a garlicky odor. Very soluble in carbon disulphide, sparingly soluble in alcohol, ether, fats, ethereal oil and bile, but almost insoluble in water. It emits luminous vapors in the dark and catches fire spontaneously. **Dose:**—0.0005 to 0.001 G. Br. ($\frac{1}{80}$ to $\frac{1}{100}$ grain). Average (U.S.P.), **0.0005 G.**

Pilulæ Phosphori (U.S.P.), each pill contains 0.0006 G. of phosphorus. **Dose:**—1 to 2 pills. Average (U.S.P.), 1 pill.

Oleum Phosphoratum (B.P.), contains 1 per cent. phosphorus in oil of almond. **Dose:**—0.005 to 0.01 c.c. Br. ($\frac{1}{6}$ to $\frac{1}{10}$ ♏).

GROUP OF SULPHUR AND SULPHIDES.

This group contains **SULPHUR, HYDROGEN SULPHIDE** and the **ALKALI SULPHIDES.**

SULPHUR itself has no action whatsoever, as it is insoluble in the fluids of the body and is consequently not absorbed. When given by the mouth or applied locally in the form of ointments, it is slowly **transformed** with the formation of hydrogen sulphide and alkali sulphides so that its action is entirely dependent upon these.

In the **gastro-intestinal tract,** their irritant effect causes an increased peristalsis with mild purgation. The stools are, as a rule, mushy and seldom liquid because the sulphides which are the active agents are formed very slowly from sulphur. On the **skin** in the form of ointment the latter acts as a stimulant and also as an antiseptic and parasiticide.

HYDROGEN SULPHIDE produces marked **local irritant action** which, when inhaled, may lead to burning of the eyes with formation of tears, running of the nose, pharyngitis, bronchitis and even œdema of the larynx.

Besides the local irritant effect, this gas produces severe constitutional poisoning referable to an action on the **central nervous system.** In fact, one part in 5000 of air may produce alarming effects.

After it is inhaled in sufficient quantity, it produces narcosis due to a depression of the brain and death from paralysis of respiration. In some cases death takes place almost immediately,

while in others, it succeeds after a few hours of narcosis and is frequently preceded by violent convulsions. The latter may occur in both mammals and frogs and are probably due to irritation of the brain, at least in the warm-blooded.

Workmen in sewers or chemists in laboratories occasionally show mild symptoms of hydrogen sulphide **poisoning:** these consist chiefly of dizziness, headache, somnolence and general weakness.

After administration by the mouth, it is only **absorbed** slowly and since it is *rapidly oxidized to sulphates* enough is never present in the blood at one time to produce severe poisoning. A small amount, however, is **excreted** as hydrogen sulphide by the breath, and imparts to the latter a disagreeable odor. It is a strong protoplasmic poison and easily kills the lower forms of organisms both vegetable and animal.

The **ALKALI SULPHIDES** produce the same effects as hydrogen sulphide, but in addition they are also strong alkaline caustics. They dissolve horny tissues, especially the upper layers of **epidermis** and the hairs. Large quantities injected intravenously transform **hæmoglobin** to sulpho-methæmoglobin, a compound which imparts to the blood a dark brown color with a greenish hue.

They depress the **central nervous system** just as hydrogen sulphide, and after narcosis and convulsions produce death from paralysis of the medulla. They, however, do not seriously affect the heart. Like the latter, they are chiefly oxidized to sulphates and excreted as such by the urine, yet a small portion leaves by the lungs in the form of hydrogen sulphide.

SUMMARY OF GROUP ACTION.—*Local caustic, irritant and antiseptic action. In the intestines cause laxative effect. On skin produce stimulation and kill parasites. Nearly all the central nervous system depressed and death due to medullary paralysis. Convulsive centres in brain may be stimulated.*

THERAPEUTIC APPLICATION.—**Sulphur** itself is used internally as a *laxative in piles, constipation*, etc., on account of the local irritant action of the hydrogen sulphide and alkaline sul-

phides evolved. It is mild because these are formed but slowly, and, therefore, it produces only soft mushy stools, but not violent purgation.

It is used locally in the form of an ointment, as an antiseptic against *scabies* and other *skin parasites*, also as a stimulant in indolent forms of dermal affections.

Potassium and **calcium sulphides** are used mainly as *external caustics*. The latter are sometimes used internally for certain skin diseases. Both are employed in preparations used for removing superfluous hair.

Hydrogen sulphide was formerly injected into the rectum for *pulmonary tuberculosis* with the hope that during the excretion by the lungs it would kill the organisms. This method of treatment has not proved successful and is exceedingly disagreeable. It is used externally in the form of sulphur baths for *rheumatism* and other chronic diseases.

MATERIA MEDICA.

Sulphur Sublimatum (U.S.P., B.P.), or sublime sulphur, fine, yellow powder, having a slight odor, insoluble in water, almost insoluble in alcohol, but soluble in benzine.

Sulphur Præcipitatum (U.S.P., B.P.), or precipitated sulphur, fine, amorphous powder, lighter than the above. Same properties.

Sulphur Lotum (U.S.P.), or washed sulphur, fine yellow powder, same properties as the above. **Dose:**—Of sulphur 1.0 to 5.0 G. Br. (15 to 45 grains). Average (U.S.P.), **4.0 G.**

Unguentum Sulphuris (U.S.P., B.P.), contains 15 per cent. sulphur.

Calx Sulphurata (U.S.P., B.P.), contains about 60 per cent. calcium sulphide. It is a pale, greyish powder, with a faint odor of hydrogen sulphide, having an alkaline taste. Gradually decomposed by exposure to the air. Very slightly soluble in water, insoluble in alcohol. **Dose:**—0.005 to 0.05 G. Br. ($\frac{1}{10}$ to 1 grain). Average (U.S.P.), **0.065 G.**

Potassa Sulphurata (B.P.), or liver of sulphur, composed of a mixture of potassium sulphide and potassium hyposulphite. It consists of irregular pieces of a liver-brown color which absorb oxygen and carbon dioxide on exposure to the air, and change to a greenish-yellow, and finally to a greyish mass. It has a faint odor of hydrogen sulphide, and a bitter, alkaline taste. It is soluble in 2 parts of water.

Sulphuris Iodidum (U.S.P.), brittle masses, greyish-black color, with a metallic lustre, having the odor of iodine and an acrid taste. Almost insoluble in water. **Dose:**—0.05 to 0.2 G.

COMPOUNDS OF HEAVY METALS.

When solutions of the heavy metals are brought into contact with albumins, they form together a precipitate of the latter. With some, as copper and zinc, this precipitate is tough, dense and insoluble; with others, as mercury, arsenic and gold, it is less tough and easily redissolved in an excess of albumin.

Those metals which form insoluble albuminates only destroy the cells in strong solution by coagulating their albumin and, therefore, act as superficial caustics, but in dilute solution they are powerful astringents. On the other hand, those which form soluble compounds with proteids penetrate deeply into the tissue and form deep caustics, but not astringents.

Although the main part of the action of a metallic salt is due to the dissociated metal or metalic oxide ions, yet the salts with the stronger acids owe a part of their action to the dissociated acid ions.

The salts of the metals, with some of the organic acids and other compounds which are difficultly dissociated, have very weak action, while those in combination with strong acids, as nitric, hydrochloric and sulphuric, may act as strong caustics, partly on account of the strength of the liberated acid and partly because these compounds are easily dissociated.

All metallic salts are antiseptics. This action is mainly due to the affinity of the metal for the albumin constituent of bacterial cells.

With few exceptions, metals are difficultly absorbed from the gastro-intestinal tract; so that *poisoning after the ingestion* is due to inflammation or corrosion of the alimentary canal. The following exceptions are arsenic which is absorbed and which causes both severe, acute and chronic constitutional symptoms; lead and mercury which can produce, after their absorption, marked subacute and chronic constitutional symptoms. The others are absorbed in traces, but not in sufficient quantities to give rise to general symptoms.

The metals are *slowly excreted* by the gastro-intestinal mucous

membranes, liver and kidneys, as albuminates. They may, as copper and silver, become stored up in organs for life.

When injected directly into the circulation in the form of double salts or soluble albuminates, all metals produce gastro-intestinal symptoms, also stimulation or depression of the central nervous system and heart, and irritation of the excretory organs which are mainly the gastro-intestinal tract and the kidneys.

GROUP OF ALUMINUM.

Although not a heavy metal, **ALUMINUM** is best grouped in this series on account of its pharmacological action.

When brought in contact with a denuded surface or with a mucous membrane, aluminum preparations precipitate a tough layer of aluminum albuminate; thus they act strongly as **astringents,** i. e., they check secretions and contract the vessels. Like all agents of this class, if applied in too concentrated form or over a prolonged period of time, they produce irritation and inflammation.

The **poisoning** after ingestion by the mouth, is due only to the local irritant action upon the mucous membranes of the gastro-intestinal tract, and consists of symptoms of gastro-enteritis. Aluminum salts are not absorbed by the stomach and intestines so that they do not produce constitutional poisoning even after taking internally for months. They are never found in the **urine** and cause no change in the metabolism.

When given subcutaneously or intravenously in the form of double salts, aluminum does not produce any **symptoms** before three or four days. These consist of great weakness, tremors, clonic convulsions, then paralysis of the limbs, somnolence, albuminuria, vomiting and great loss of weight, at first obstinate constipation, usually followed just before death by diarrhœa.

The symptoms are due to a stimulation of certain parts of the central nervous system followed by paralysis of the same, secondary to a degeneration of the nerve cells and fibres of the medulla and cord and to the irritation at the places of excretion, the gas-

tro-intestinal tract and kidneys. Both these and the liver may also show signs of *fatty degeneration.*

TIN, like aluminum, is not absorbed from the unbroken mucous membrane, and has no constitutional action after internal administration. When given intravenously or subcutaneously in the form of double salts, it causes, in two to three days, symptoms of general weakness; then convulsions, vomiting, diarrhœa and death follow in two or three more days from paralysis of the central nervous system. Tin poisoning in man is unknown, therefore there is no danger in the use of kitchen utensils made of this metal.

MOLYBDEN, TUNGSTEN, VANADIUM, BERYLLIUM and **URANIUM** induce only the ordinary metallic poisoning in animals. In addition uranium causes glycosuria and diminution in bodily oxidation.

SUMMARY OF GROUP ACTION.—*Strong local astringent effect due to the formation of insoluble compounds with proteids. Not absorbed by the gastro-intestinal tract. No constitutional poisoning after administration by this channel. After intravenous injection symptoms of paralysis of central nervous system due to degeneration of the same and also irritation and degeneration of the gastro-intestinal tract where aluminum is excreted.*

THERAPEUTIC APPLICATION.—The main uses of **aluminum** preparations are as *astringents*, *hemostatics* and *antiseptics* over wounds and inflamed mucous membranes, as those of the vagina, urethra, rectum, mouth, and pharynx.

Alum and aluminum hydrate are sometimes used internally in small doses to check *diarrhœa*, and in large ones as *emetics.*

MATERIA MEDICA.

Alumen (U.S.P., B.P.), or aluminum and potassium sulphate, or alum, colorless crystals, having a sweetish and strongly astringent taste. Soluble in 9 parts of water, insoluble in alcohol. Used externally in ¼ to 3 per cent. solutions. **Dose:**—0.3 to 1.0 G. Br. (5 to 15 grains). Average (U.S.P.), 0.5 G.

Alumen Exsiccatum (U.S.P.), or burnt alum. White granular powder, without odor, but with a sweet astringent taste, and hygroscopic in the air. Slowly soluble in 20 parts of water. **Dose:**—0.3 to 1.0 G.

Alumini Hydras (U.S.P.), a white, amorphous powder, odorless and tasteless, permanent in the air, insoluble in water and alcohol. **Dose:**—0.3 to 1.0 G.

Alumini Sulphas (U.S.P.), white, crystalline powder, without odor, with a sweetish astringent taste. Soluble in 1.2 parts of water, almost insoluble in alcohol. Used externally in ¼ to 3 per cent. solution.

Alumini Chloridum, white crystals, soluble in water and alcohol, hygroscopic and unstable, liberates hydrochloric acid.

Alumnol, betanapthol disulphonate of aluminum, white powder, soluble in water used in ¼ to 3 per cent. solution.

GROUP OF COPPER AND ZINC.

Locally upon mucous membranes or denuded surfaces, solutions of **COPPER** and **ZINC** form a superficial layer of difficultly soluble albuminous compounds and, therefore, act as **astringents.**

The salts with the stronger acids, which are easily dissociated, act in greater concentration as *irritants and caustics.*

Both the sulphates of copper and zinc have a strong local action but the chlorides of both are still more active and especially that of zinc. On the other hand the albuminous combinations of these metals and the oxide and carbonate of zinc which are soluble with difficulty, have a much less marked local effect.

After internal administration of large doses of soluble salts, the **symptoms** are those of gastro-intestinal irritation, *i. e.*, vomiting, purging which may be bloody, and violent pain in the abdomen. Death takes place in collapse from the severity of the *inflammation of the alimentary canal*, and the mucous membrane of the latter shows great congestion and ecchymoses. With moderate doses, however, these serious symptoms do not occur, especially with sulphates as they cause emesis before inflammation begins and are quickly removed. This **vomiting,** which is almost constant, is due to direct irritation of the gastric mucous membrane because it does not occur after subcutaneous administration.

Although the salts of both copper and zinc are **absorbed** by the stomach and bowels, yet they *never produce constitutional poisoning after ingestion* as they are rapidly removed from the blood by different parenchymatous organs, especially the liver,

but also the kidneys, spleen and thyroid. This takes place quicker than the absorption which diminishes in proportion to the size of the dose. A certain quantity of copper may remain *stored in the liver* for many years and in fact, it is often regarded as a normal constituent in minute quantities.

Both metals are **excreted** by the bile, urine, salivary, gastric and intestinal secretions; copper is chiefly eliminated by the liver and kidneys while zinc prefers the alimentary tract.

Administered subcutaneously or intravenously as double compounds, they produce paralysis of the **central nervous system,** heart and striated muscles. Copper acts much more energetically on the two latter but zinc, on the other hand, depresses more the former. Both form special compounds with the **hæmoglobin** of the blood called cupro-hæmol and zinc-hæmol. In fact, in some of the lower animals copper is found normally instead of iron combined with their blood coloring matters, and in most animals, it is found in traces as a normal constituent of the liver.

If death does not take place immediately from the action on the vital organs, irritation of the excretory channels, as the gastro-intestinal tract and kidneys, may be observed, and with zinc, vomiting may even occur after subcutaneous administration on account of the inflammation of the stomach resulting from the metal there excreted.

No true **chronic constitutional poisoning** occurs from either metals even if the dose ingested is large. The only symptoms observed are those referable to long-continued irritation of the gastro-intestinal tract and consist of a decrease of appetite, nausea, vomiting and diarrhœa. Sometimes these have been seen in workmen in brass factories and in other individuals after eating canned peas or beans containing copper to preserve the green color of the chlorophyl. From inhaling the dust of either metal occasionally, laryngitis, pharyngitis and bronchitis may be produced. In people working with zinc sometimes a strange condition called *brassfounder's ague* develops. This consists of soreness of the chest, coughing, general malaise, pain throughout the body, and also chills followed by a rapid heart beat. The

patient after breaking out into perspiration goes to sleep and wakes up perfectly well. Copper often imparts a greenish tinge to the hair, skin and gums of workers.

Some plants, as grape-vines, are benefited by the application of copper. On the other hand, many lower forms, as bacteria, tubifex and tadpoles are killed by a very minute amount. Copper is said to be a good antiseptic in less than 1 per cent. solution.

Cadmium salts differ but little from those of zinc in their action.

SUMMARY OF GROUP ACTION.—*In dilute solutions, astringent action, but in concentrated form, caustics. Internal administration gives rise to vomiting and at times to gastro-enteritis but never constitutional poisoning. Absorbed slowly by alimentary canal and separated from the blood by liver, spleen, kidneys and thyroid. Form compounds with hæmoglobin. After intravenous injection, paralysis of central nervous system, heart and muscles. Poisonous to many lower forms, therefore, antiseptics.*

THERAPEUTIC APPLICATION.—Salts of **copper** and **zinc** are used in dilute solutions mainly as *astringents, hemostatics* and *antiseptics* over inflamed mucous membranes and denuded surfaces, especially in gonorrheal inflammations of the urethra and vagina.

They are employed in concentrated solutions or in the solid forms as *caustics* over exuberant granulations and to destroy new growths. Zinc chloride, which is often one of the main constituents in so-called "cancer cures," has now been used with a good deal of success in legitimate practice as a caustic to treat cancer of the neck of the uterus. It does not produce a cure but may prolong life.

Zinc and copper sulphate were used in the past in small doses as astringents in *diarrhœa*, but have nowadays been replaced by the newer tannin preparations.

They were also employed in large doses on account of their irritant action as *emetics*, but have been superseded by apomorphine.

MATERIA MEDICA.

Cupri Sulphas (U.S.P., B.P.), blue vitriol, transparent blue crystals, with a nauseous metallic taste, soluble in 2.6 parts of water, almost insoluble in alcohol. Used externally in $\frac{1}{10}$ to $\frac{1}{2}$ per cent. solution. **Dose:**—0.1 to 1.0 G. Br. (2–15 grains). Average (U.S.P.), astringent **0.01 G.**, emetic **0.25 G.**

Zinci Sulphas (U.S.P., B.P.), white, odorless crystals with an astringent, metallic taste, soluble in water, insoluble in alcohol. Used externally in $\frac{1}{10}$ to $\frac{1}{2}$ per cent. solution. **Dose:**—0.5 to 2.0 G. Br. (3–30 grains). Average (U.S.P.), **1.0 G.**

Zinci Chloridum (U.S.P., B.P.), white granular powder, intensely caustic properties, very astringent metallic taste, very deliquescent, very soluble in water and alcohol.

Liquor Zinc Chloridi (U.S.P., B.P.), contains 36 per cent. by weight of chloride of zinc.

Zinci Oxidum (U.S.P., B.P.), amorphous white, tasteless powder, insoluble in water and alcohol. **Dose,** Br. (2–10 grains). Average (U.S.P.), **0.25 G.**

Unguentum Zinci Oxidi (U.S.P.), contains 20 per cent. and Unguentum Zinci (B.P.), contains 15 per cent. of zinc oxide.

Zinci Acetas (U.S.P., B.P.), white crystals, having a faintly acid odor and astringent, metallic taste. Soluble in 2.7 parts of water, in 36 parts of alcohol. **Dose,** Br. (1–3 grains). Average (U.S.P.), **0.125 G.**

Zinci Valeras (U.S.P.), Zinci Valerianas (B.P.), white, pearly scales with the odor of valerianic acid, and a sweetish, astringent, metallic taste. Soluble in 100 parts of water and 40 parts of alcohol. **Dose:**—0.05 to 0.3 G. Br. (1–3 grains). Average (U.S.P.), **0.125 G.**

GROUP OF BISMUTH.

Almost all the salts of **BISMUTH** used in medicine are insoluble in water, but some of these become gradually decomposed in contact with the tissues of the body upon which they exert an astringent action, both in virtue of the metallic and of the acid constituents. The most commonly used compound of bismuth, the subnitrate, causes this astringent effect partly through the liberated nitric acid which is even formed in watery suspension without contact with living tissues. The decomposition is slow, therefore the action is mild and prolonged.

Insoluble bismuth preparations are only slowly **absorbed** from the gastro-intestinal tract so that in moderate doses constitutional poisoning does not occur after ingestion. Being insoluble and so slowly dissociated, they can hardly be given in concentration great enough by the mouth to cause gastro-intestinal irrita-

tion. There are reasons to believe that bismuth preparations stimulate the secretion of gastric mucus and this might explain their good effect in hyperacidities of the stomach. In these conditions where the normal protective alkaline mucus is thought to be deficient, it would be restored, and at the same time the too acid gastric juice would be partly neutralized by the alkaline mucus.

In individuals with diarrhœa, they often stop this symptom. They always darken the stool to a slate brown color. This condition is due to the formation of the sulphide and oxide of bismuth.

Numerous cases of **poisoning** formerly reported after the internal administration of bismuth preparations have been found to be due to arsenic, antimony and lead formerly found as impurities in bismuth preparations. The bad odor of the breath which they cause is due to traces of tellurium. When applied to wounds or to serous surfaces, absorption of bismuth seems to be better and constitutional poisoning has occurred occasionally in human beings. It consists of inflammation of the entire alimentary tract, stomatitis, ulceration and swelling of the gums and tongue, pharynx, œsophagus, marked inflammation and even ulceration of the stomach, especially of the large intestines and cæcum, also albuminuria, due to inflammation of the kidneys. On account of these conditions, there is pain on swallowing and also tenderness of the abdomen, and colic, vomiting and diarrhœa, as after any gastro-intestinal irritation.

Since the use of bismuth subnitrate in large quantities for *x*-ray examination of the gastro-intestinal tract, there have been numerous cases of poisoning and a few deaths reported from poisoning by this salt. Investigation has shown that the subjects suffered from methemoglobinemia and that the cause of this was not due to the bismuth but to the acid radical. In other words, the nitric acid radical in bismuth subnitrate was reduced to the nitrite radical and **nitrite poisoning** occurred.

This nitrite poisoning has also been met after the rectal injection of bismuth subnitrate and is explained by the presence of reducing bacteria in the intestines. This has been found, par-

ticularly in diarrhœal trouble and in children's feces. The moral to be deducted is that we should use in preference to the subnitrate, some other salt of bismuth, as the subcarbonate. In *x*-ray work, some who still believe that the poisoning results purely from the bismuth ion, use instead barium sulphate or magnetic iron oxide.

The **alimentary canal,** particularly the large intestines, cæcum and the kidneys are especially prone to the poisonous effects of bismuth, because they are its chief organs of excretion. Yet a certain amount is separated by the liver and stored there for a time. This may explain the absence of poisoning after ingestion.

When double salts of bismuth are injected subcutaneously and intravenously in sufficient quantities, the symptoms are those, at first, of stimulation of the **cord** and **medulla,** attended with convulsions, succeeded by paralysis of these parts and death due to *respiratory and heart failure.*

The injection of repeated small doses in animals produces the same subacute or chronic poisoning seen in man after accidental absorption.

TELLURIUM and **SELENIUM** have in general the characteristic action of the heavy metals. They produce by subcutaneous injection, irritation of the gastro-intestinal tract and kidneys, and paralysis of the central nervous system and heart. When taken internally, even in traces, they impart to the breath a garlicky odor. The salts are reduced in the body to the metallic state and then combined with methyl in the form of volatile odorous compounds which are excreted by the lungs, kidneys and intestinal tract.

Tellurates paralyze the ending of the sweat glands like atropine and agaric acid.

SUMMARY OF GROUP ACTION.—*Insoluble salts become gradually decomposed in contact with living tissues and by virtue of both the basic and acid ions act as astringents and antiseptics. Almost unabsorbed by oral administration, therefore, seldom poisonous action even with large internal doses, except from nitrate salts which cause nitrite poisoning. Absorbed much more readily from serous*

surfaces as joints, and symptoms of marked gastro-intestinal and renal irritation may ensue because of excretion by kidneys and bowels. When injected into circulation, produce first stimulation then depression of the central nervous system. Death results from paralysis of respiration and circulation.

THERAPEUTIC APPLICATION.—Bismuth salts are used in inflammatory and *ulcerative conditions* of the stomach and intestines: the good effect in such cases is due to the astringent plus the protective effect. The latter comes from the formation of a coating over the ulcer, by virtue of the insolubility of the salts commonly in use.

They have been used as astringents in *catarrhal inflammations* of practically all mucous membranes as those of the urethra, vagina and gastro-intestinal tract and are of great value in arresting *diarrhœa*. They are also of value in *skin diseases* in the form of ointments.

The subnitrate, but especially the other salts of bismuth with antiseptic radicles as naphthol, phenol and salicylic acid, are used as disinfectants of the gastro-intestinal tract.

The **subcarbonate** is the best salt to use in gastric affections, while the salicylate, naphtholate, etc., are more valuable as intestinal antiseptics. The subnitrate should never be used in huge doses for fear of nitrite poisoning.

MATERIA MEDICA.

Bismuthi Subnitras (U.S.P., B.P.), white, heavy, odorless, tasteless powder, insoluble in water and alcohol. It becomes gradually decomposed in watery suspension with the liberation of free nitric acid. **Dose:**—0.5 to 3.0 G. up to 30.0 G. in 24 hours. Br. (5–30 grains). Average (U.S.P.), **0.5 G.**

Bismuthi Subcarbonas (U.S.P., B.P.), white, heavy, odorless, tasteless powder, insoluble in water and alcohol. **Dose:**—0.5 to 3.0 G., up to 30.0 G. in 24 hours. Br. (5–30 grains). Average (U.S.P.), **0.5 G.**

Bismuthi et Ammonii Citras (U.S.P.), white scales, with a metallic taste, very soluble in water, soluble in alcohol. **Dose:**—0.1 to 0.3 G. Average (U.S.P.), **0.125 G.**

Bismuthi Citras (U.S.P.), a white powder, insoluble in water, and alcohol. **Dose:**—0.05 to 0.2 G. Average (U.S.P.), **0.125 G.**

Bismuthi Subgallas (U.S.P.), or dermatol, yellow, odorless powder, insoluble in water and alcohol. **Dose:**—0.1 to 0.2 G. Average (U.S.P.), **0.25 G.**

Bismuthi Subsalicylas (U.S.P.), Bismuthi Salicylas (B.P.), cream colored powder, insoluble in water and alcohol. **Dose:**—0.5 to 3.0 G. up to 30 G. in 24 hours. Br. (5 to 30 grains). Average (U.S.P.), **0.25 G.**

Bismuthi Betanaphtholas or Orpholum, greyish powder with unpleasant taste and odor of naphthol, containing 74 per cent. bismuth. **Dose:**—1.0 G.

Bismutose (bismuth albuminate), white, insoluble powder without odor and taste. Contains 22 per cent. bismuth. **Dose:**—1.0 to 2.0 G.

Bismon (colloidal bismuth). Compounds of lysalbinic and protalbinic acids with oxides of bismuth. Soluble in hot and cold water, giving yellowish-red opalescence. Contains 25 per cent. bismuth.

Xeroform (bismuth tribromphenol), yellow powder containing 60 per cent. bismuth, insoluble in water. **Dose:**—0.5 G.

GROUP OF LEAD.

LEAD is one of the few metals which *produces constitutional symptoms after internal administration.* These are always chronic in nature, because they are due to the gradual accumulation of the metal in the system on account of its more rapid absorption than excretion. They result as a rule from the administration of small doses of any lead salts over a certain period of time, and but rarely follow the ingestion of one large dose.

The **absorption,** although slow, is more rapid than that of any other metal, except mercury. Even the most insoluble sulphate and metallic lead become slowly dissolved and absorbed by the alimentary canal. The latter is probably the chief channel of absorption, although wounds and mucous membranes of the urethra and vagina may take up enough to cause a constitutional action. The unbroken skin probably does not absorb lead preparations and the poisoning seen in painters is due to handling food with uncleanly hands and also to the entrance of the lead paint into cuts or abrasions.

Locally applied in not too concentrated form to abraded surfaces or mucous membranes, solutions of lead salts, as the acetates, form a dense precipitate of albuminate and thus act as **astringents** and **hemostatics.** On account of their affinity for albumin, they act as **antiseptics** but not as much as many other metals, probably because the lead ions are not so poisonous to

lower forms. Concentrated solutions of easily dissociated lead salts act as irritants but rarely as caustics.

Large doses given by the mouth produce the ordinary **symptoms** of *gastro-enteritis*, consisting of nausea, vomiting, pain in the bowels, diarrhœa and at last collapse. The vomiting and diarrhœa may be profuse and bloody. Occasionally, chronic poisoning has resulted in persons who recovered from the acute inflammation of the alimentary canal.

Small doses given over a long period of time produce a chronic condition of poisoning characterized by irritation of the alimentary canal, kidneys, central and peripheral nervous and muscular systems. These symptoms of stimulation are followed by depression and degeneration of all those different organs. It also produces changes in the **blood** resulting in anæmia and in the general metabolism causing gout. Among the first symptoms of **chronic lead poisoning** are those referable to the gastro-intestinal tract. It is not surprising, as this tract comes most in contact with the metal, both during absorption and **excretion.** It leaves the body by the saliva, bile, intestinal mucous membranes and kidneys. These symptoms consist of a metallic taste in the mouth, fetid breath, sometimes a blue line on the gums, loss of appetite, nausea, vomiting, tenderness of the abdomen, and characteristic attacks of colics usually accompanied with constipation, rarely with diarrhœa.

The effect on the mouth is due to its excretion by the saliva. The gastric symptoms result from the local action of lead on the stomach mucous membrane. The latter may even at times show fatty degeneration and connective tissue proliferation.

The **colics** are paroxysmal, very severe, and often relieved by firm pressure and by atropine. They are due mainly to a powerful spasmodic contraction of the smooth muscles of the intestines dependent upon the stimulation of their nerve supply. The fact that they are relieved by atropine supports this view.

On account of the contraction of the intestines, the *vessels of the splanchnic area* are squeezed so that they hold less blood and, therefore, the general blood pressure rises. Either due to this

increased pressure in the arterial system or to direct action of the lead on the vessel parenchyma, *arterio-sclerosis* often results from chronic lead poisoning. The **kidneys,** which excrete part of the lead, also undergo degeneration mainly of a mixed parenchymatous and interstitial type.

The **brain** at times shows changes, sometimes of stimulation, as sleeplessness, headaches, epileptic and choreiform seizures, maniacal delirium, hallucinations, sometimes symptoms of depression, as great weakness and stupor.

The **peripheral nerves** also show signs of irritation in the form of severe lancinating pains about the joints. The long-continued inflammation of the peripheral nerves leads to their degeneration and paralysis. It is especially apt to affect those going to the extensors, so the characteristic "wrist-drop" (inability to hold up the hand), is often seen resulting from paralysis of the extensors of the arm which are affected sooner than the flexors.

Anæsthesia of the skin occurs from degeneration of the sensory nerves. Blindness occasionally results from optic atrophy. Deafness which sometimes occurs, is probably also due to changes in the specific nerve of hearing.

The **muscles** also become affected and lose the irritability to induced currents but react more strongly to direct ones, thus showing the reaction of degeneration.

When suitable preparations of lead are injected into the circulation of animals, the symptoms are referable to many of the organs which are affected in human beings in chronic poisoning. They consist of irritation of the gastro-intestinal tract with the characteristic colics, muscular paralysis and the cerebral changes giving rise to tremors, epileptiform convulsions and also mental apathy.

Acute poisoning from lead is treated by neutralizing the poison in the gastro-intestinal tract with dilute sulphate solutions in order to make an insoluble salt which is then removed by washing out the stomach and by purging, for if this is not done it will gradually become absorbed. White of egg is also useful on account of the nearly insoluble albuminate which is formed.

Chronic poisoning is usually treated by detecting and removing the source of contamination. The elimination is furthered by the administration of potassium iodide and different diuretics and laxatives. Atropine is given to relieve the colics. The anæmia is corrected by iron and the general health is improved by every method at hand. If irritated brain symptoms are present, they may be checked by narcotics. Paralysis may be treated with strychnine, massage and electricity.

THALLIUM salts resemble in their action those of lead but are more poisonous. They are said to produce special atrophy of the muscles in animals and baldness in man.

SUMMARY OF GROUP ACTION.—*Local effect, astringent. After internal administration of a large dose, the symptoms consist of acute gastro-enteritis. When small amounts are ingested over a period of time, symptoms are irritation of the gastro-intestinal tract with loss of appetite, nausea, vomiting and colics, with obstinate constipation, peripheral neuritis with pain and paralysis, "wrist drop," cerebral symptoms, degeneration of blood vessels and kidneys, anæmia, predisposition to gout. Occasionally a blue line exists at the junction of the teeth and gums.*

THERAPEUTIC APPLICATION.—**Lead** is used almost exclusively in the form of a solution of the acetate as an *astringent* and *hæmostatic* over abraded surfaces and inflamed mucous membranes, as those of the urethra and vagina, etc., and also for itching *skin affections.*

Formerly it was employed more than at present internally to check *diarrhœa.* Its use in the past for hemorrhage in remote parts as the lungs and kidneys was obviously irrational.

It should not be given over a prolonged period of time, either as injections or internally, for fear of chronic poisoning.

MATERIA MEDICA.

Plumbum Oxidum (U.S.P., B.P.), or litharge; yellowish-red powder, insoluble in water, soluble in nitric and acetic acid. Used for making the plaster of lead and the lead acetate.

Emplastrum Plumbi (U.S.P., B.P.), or diachylon plaster.

Plumbi Acetas (U.S.P., B.P.), or sugar of lead, colorless, heavy crystals with a faintly acetous odor and a sweetish astringent taste. Efflorescent

and absorbs carbon dioxide on exposure to the air. Soluble in 1.8 parts of water. **Dose**:—0.05 to 0.1 G. Br. (1–5 grains). Average (U.S.P.), 0.065 G.

Liquor Plumbi Subacetatis (U.S.P.), or Goulard's extract, contains 25 per cent. lead subacetate in watery solution.

Liquor Plumbi Subacetatis Dilutus (U.S.P., B.P.), contains 3 per cent. of the above.

Ceratum Plumbi Subacetatis (U.S.P.), contains 20 per cent. of Goulard's extract, with 2 per cent. camphor.

Plumbi Iodidum (U.S.P.), bright yellow powder, without odor or taste, only soluble in about 2,000 parts of water.

Unguentum Plumbi Iodidi (U.S.P., B.P.), contains 10 per cent. lead iodide.

GROUP OF MERCURY.

MERCURY, or quicksilver, forms albuminous compounds soluble in salt solution or in an excess of albumen such as is present in body fluids. It is the most easily absorbed metal and, therefore, gives rise to definite constitutional symptoms which last over a prolonged period of time because of its slow excretion.

On account of its affinity for albumins and of its deleterious effect on living **protoplasm** mercury is an irritant and antiseptic. Its action varies greatly on different germs but it is one of the most active of the antibacterial metals. Since the time of Paracelsus, it was known that mercury frequently influenced the disease syphilis, but it was only of very recent date that a specific action against syphilis has been proved by Metchnikoff. He found that if a subject is inoculated with the virus containing the spirochæta pallida and the site of inoculation is treated with an ointment of calomel within twenty minutes, no infection occurs. Yet it has very little action on the *unorganized ferments* such as pepsin and pancreatin, and unless the concentration is sufficient to precipitate the ferments it does not alter the digestion. Calomel, an insoluble salt of mercury, does not check digestion even in large doses, but hinders markedly putrefactive decomposition in the intestines; thus the stools are frequently green after this drug, due to the fresh pigment preserved from destruction by the sterilization of the alimentary canal.

Since mercury forms soluble compounds with proteids it penetrates deeply into living tissue and therefore acts rather as a **caus-**

tic than as an astringent. With the salts of this metal as with those of others the local action is partly dependent on the acid ions and varies in intensity with the caustic power of the acid constituent and its ease of dissociation. When any salt of mercury is injected subcutaneously or intramuscularly there is always a great deal of pain and inflammatory reaction.

Mercury in all its different forms, as soluble and insoluble compounds, and even in the metallic state, is **absorbed** by living organisms. It may enter the system by all channels, gastro-intestinal tract, epidermis, subcutaneous and muscular tissues and lungs. Both soluble and insoluble inorganic compounds are in part or wholly transformed to albuminates before absorption. Thus even the metallic form rubbed into the skin in a fine state of subdivision mixed with fat is absorbed partly as an albuminate and partly in combination with fatty acids. When the element is taken internally in a finely divided condition it is probably dissolved by acids in the gastro-intestinal tract and passes into the circulation combined with proteids. That which is absorbed as fumes by the lungs or the skin probably also becomes transformed to albuminates during its absorption.

When strong solutions of mercurial compounds are given by the mouth, **acute poisoning** follows with the symptoms of *gastro-enteritis*, as burning in the mouth, throat, œsophagus, violent griping pains in the abdomen, nausea, vomiting and diarrhœa (both the latter may be bloody with shreds of mucous membrane), anuria, cold clammy skin, small irregular pulse, decreased respiration and collapse. The acute form of poisoning has in a few instances followed absorption from wounds or from the vagina after too concentrated corrosive sublimate douches. Last year, several cases were reported of acute constitutional poisoning followed by death after the introduction of solid corrosive sublimate tablets into the vagina by ignorant women with the object of producing abortion. Poisoning from local application is practically identical with the internal except that the corrosion of the mouth is less marked at first. Chronic symptoms may follow if the subject survives.

Occasionally, chronic poisoning results from one or two doses

which are insufficient to produce acute symptoms. But, as a rule, it occurs when small doses are administered by any channel of absorption over a long period of time. The **chronic symptoms of poisoning** are seen principally in the gastro-intestinal tract where mercury is in part **excreted.** Also passing out of the body by the saliva it produces irritation of the whole mouth, resulting in swelling of the salivary glands, great salivation, fetid breath, swelling of the tongue and gums, even with ulceration and necrosis of the latter which may extend to the jaw, and dropping out of the teeth.

Some is excreted by the gastric juice, but in much larger quantities by the intestines and especially the large ones where it produces its most marked action. In small doses it may produce simple hyperemia of the gastro-intestinal tract and increased intestinal peristalsis attended with loose movements. In larger doses, it causes well marked inflammation and even ulceration and sloughing, most marked in the large intestines. Since it is excreted also by the kidneys, it occasions severe inflammation and degeneration of these organs and, in a characteristic way, the necrotic, degenerated cells of the tubules become filled with deposits of calcium phosphate. Mercury is also found in the perspiration and this may account for the skin eruptions sometimes observed after prolonged administration. Besides these symptoms of irritation of the excretory channels there are others referable to the central and peripheral nervous systems.

On account of its action on the **central nervous system,** it produces a state of great nervous irritability, timidity, hallucinations, sometimes delirium, attended by sleeplessness, headaches and tremors (mercurial erythism). It causes a **peripheral neuritis,** especially affecting the myelin sheath of the nerves and thus occasioning sharp pains in the extremities and various paralyses, but the muscles remain undegenerated with intact electrical reaction. This forms a striking difference from the lead and arsenic neuritis.

At first the **metabolism** is beneficially changed, the subject gains weight and the **hæmoglobin** of the blood is increased,

probably through hyperemia of the bone marrow. Later the opposite symptoms occur, loss of weight, anæmia, cachexia and death in general marasmus. The improvement in body weight and in the blood is especially well seen in syphilitic subjects. The urine may also contain sugar, besides albumin and casts. In mercurial poisoning occasionally the different parenchymatous organs show evidence of fatty degeneration yet the normal fat in the tissues and bone marrow soon disappears.

Given intravenously in large doses in the form of a compound soluble in the fluids of the body, mercury produces intense irritation of the **kidneys.** The secretion of these organs, after a very temporary increase, is diminished in quantity, and there appear albumen, casts and blood and lastly total suppression. The blood pressure sinks from paralysis of the vasomotors and heart and death ensues. Formerly mercurial preparations were said to stimulate the flow of bile, but direct experiments have never shown any such effects even though they are in part excreted by the liver.

The **excretion** of mercury which is very slow takes place chiefly in the urine, saliva, gastric and intestinal secretions and in traces in the bile, perspiration, milk and also from the placental circulation into the fœtus in pregnant women.

SUMMARY OF GROUP ACTION.—*Strong antiseptic action, also irritant and caustic. Symptoms of acute poisoning are those of gastro-enteritis and nephritis. In chronic poisoning besides the gastro-intestinal tract and kidneys, the skin, central nervous system, peripheral nerves, blood and general metabolism affected. Eliminated chiefly by intestines and kidneys.*

THERAPEUTIC APPLICATION.—The chief employment of **mercury** in medicine is in the treatment of *syphilis.* Its beneficial action, which in some cases is quite wonderful, is probably due both to its influence on metabolism and to a specific effect on the Treponema pallida, the causal agent of the disease. The fact that many cases of syphilis are cured of the primary and secondary symptoms simply by improving their metabolism through hygienic means and other measures without mercury leads us to

infer that at least some of the action of mercury may be due to its influence on nutrition; but on the other hand, the occurrence of cases where all hygienic measures and other means used to alter the metabolism have failed, but where the use of mercury brings about immediate improvement, lead us to believe that mercury acts at least to some extent by influencing the specific cause of syphilis. It is used in the treatment of this disease in almost all its forms and by all methods of administration, internally, subcutaneously, by inunction, by fumigation, inhalation, intravenously, etc.

On account of their deleterious influence upon living protoplasm, preparations of mercury are used as antiseptics internally and externally. **Corrosive sublimate** is the most commonly employed as a *surgical antiseptic* to wash wounds. **Calomel** has the preference as an intestinal antiseptic. Almost all forms of mercury are employed in the form of ointments as disinfectants and irritants in various *skin diseases*. For pediculi pubis, **blue ointment** is especially used. Calomel is frequently dusted on syphilitic *chancres*.

Mercurials, especially calomel, are given as *purgatives* on account of the stimulant action on the intestines. The latter was formerly used as a cholagogue, but it is now known not to increase the flow of bile.

Calomel has been used with success as a *diuretic* in some cases of dropsy, of cardiac and hepatic origin. The action is probably due partly to the stimulant effect on the renal epithelium, and possibly partly to some action on serous membranes causing the absorption of fluids. It has been observed to produce diuresis in some cases of renal dropsy, but if used at all in these cases it must be given with extreme caution on account of its local effects on the kidneys.

MATERIA MEDICA.

Hydrargyrum cum Creta (U.S.P., B.P.), or grey powder, contains 38 per cent. of metallic mercury besides prepared chalk, honey and water. **Dose:**—0.05 to 0.5 G. Br. (2–8 grains). Average (U.S.P.), **0.25 G.**

Massa Hydrargyri (U.S.P.), or blue mass. It contains 33 per cent. of

mercury, besides honey of rose, licorice, althæa and glycerine. **Dose:**—0.05 to 0.5 G. Average (U.S.P.), **0.25 G.**

Unguentum Hydrargyri (U.S.P., B.P.), or blue butter, contains 50 per cent. of mercury. **Dose:**—1.0 to 5.0 G. by inunction. Br. (½–1 ʒ).

Unguentum Hydrargyri Diluti (U.S.P.), 33 per cent.

Emplastrum Hydrargyri (U.S.P., B.P.), contains 30 per cent. mercury.

Emplastrum Ammoniaci cum Hydrargyro (B.P.), contains 18 per cent. mercury.

Hydrargyri Oxidum Rubrum (U.S.P., B.P.), or red precipitate, orange red crystalline scales almost insoluble in water.

Unguentum Hydrargyri Oxidi Rubri (U.S.P., B.P.), contains 10 per cent. red mercuric oxide.

Hydrargyri Oxidum Flavum (U.S.P., B.P.), yellow mercuric oxide. Light orange yellow, amorphous heavy powder.

Unguentum Hydrargyri Oxidi Flavi (U.S.P., B.P.), contains 10 per cent. yellow oxide in U.S.P. and 2 per cent. in B.P.

Oleatum Hydrargyri (U.S.P.), Hydrargyri Oleas (B.P.), contains 20 per cent. of yellow oxide.

Hydrargyri Chloridum Corrosivum (U.S.P.), Hydrargyri Perchloridum (B.P.), corrosive sublimate, white crystalline body with a caustic acrid, metallic taste, soluble in 16 parts of water, 3 parts of alcohol. **Dose:**—0.001 to 0.005 G. Br. ($\frac{1}{32}$–$\frac{1}{3}$ grain). Average (U.S.P.), **0.003 G.**

Hydrargyri Chloridum Mite (U.S.P.), Hydrargyri Subchloridum (B.P.), or calomel. A white powder without odor or taste, insoluble in water. **Dose:**—0.03 to 0.3 G. up to 1.5 G. in 24 hours. Br. (½–5 grains). Average (U.S.P.), **0.125 G.**

Lotio Hydrargyri Nigra (B.P.) or black wash, made from calomel and lime water. Used as a wash for syphilitic lesions.

Lotio Hydrargyri Flava (B.P.) or yellow wash, made from lime water and corrosive sublimate. Used as a wash for syphilitic ulcers.

Pilulæ Catharticæ Compositæ (U.S.P.), contains 0.06 of calomel, besides compound extract of colocynth, extract of jalap and gamboge. **Dose:**—1 to 3 pills.

Hydrargyrum Iodidum Rubrum (U.S.P., B.P.) or red iodide of mercury. Scarlet red amorphous powder, almost insoluble in water but freely soluble in solutions of potassium iodide. **Dose:**—0.001 to 0.005 G. Br. ($\frac{1}{32}$–$\frac{1}{16}$ grain). Average (U.S.P.), **0.003 G.**

Hydrargyrum Iodidum Flavum (U.S.P.), or yellow iodide of mercury, or protoiodide of mercury. It is a bright yellow, amorphous powder, odorless and tasteless. Almost insoluble in water, insoluble in alcohol and ether. **Dose:**—0.001 to 0.005 G. Average (U.S.P.), **0.01 G.**

Unguentum Hydrargyri Nitratis (U.S.P., B.P.), or citrine ointment. It contains 7 per cent. mercury, besides free nitric acid and lard.

Hydrargyrum Ammoniatum (U.S.P., B.P.), white precipitate or ammoniated mercury. A white amorphous powder, having an earthy metallic taste. Almost insoluble in water, insoluble in alcohol.

Unguentum Hydrargyri Ammoniati (U.S.P., B.P.), contains 10 per cent. ammoniated mercury.

GROUP OF SILVER AND GOLD.

SILVER has a very strong affinity for albumen and precipitates a dense, white, insoluble albuminate which becomes gradually black by the reduction of the metal. This affinity is so powerful that in the form of easily dissociable salts as the nitrate in concentrated solutions, it acts as a strong but superficial caustic. In dilute solutions it is an **astringent,** hemostatic and antiseptic.

After internal administration, it is so slowly **absorbed** that the larger portion passes out by the fæces. The small amount which enters the circulation becomes very readily deposited in different organs either in the form of the metal or as an organic compound, but it is never present in the circulation in sufficient quantities to induce acute constitutional poisoning.

When large doses, however, are given internally, the symptoms are those of **acute gastro-enteritis,** as vomiting, defecation, pain in the mouth, œsophagus, stomach and abdomen, pinched face, thready pulse, collapse and death. After death, the mucous membrane of the alimentary canal is found inflamed and corroded, but colored dark brown or black due to reduction of the silver salt.

When small doses are given over a long period of time to human beings, no other symptoms are observed except those of **argyria.** These consist of a greyish-black coloration of the skin, due to a deposit of the silver in the corium. These deposits are also found in the gastro-intestinal tract, liver, kidneys, spleen, mesenteric lymph glands, serous membranes, gums and vessel walls. The gums at the junction of the teeth are among the first places for the deposit and show a bluish line as in lead poisoning. Throughout all organs, it is the connective tissue rather than the epithelial cells that the pigment selects, for in the skin of man none is found in the epidermis. These symptoms occur when a sum total of at least 15 G. of silver has been administered to a human being in repeated doses. Since it is probably not excreted, that administered years before counts towards forming the condition which is incurable. Most cases of argyria

have resulted from the internal administration of silver preparations in the treatment of nervous diseases as epilepsy and different cord paralyses, but some also occur from the long continued local application to the eye, nose, throat and vagina, also in workmen using silver as a pigment, as those in artificial pearl factories. Besides the general variety, there is sometimes a local form of argyria resulting from prolonged use on the skin or mucous membranes these, at the site of application, becoming permanently stained black.

When double salts of silver are injected intravenously or subcutaneously, the main action is at first a stimulation of the **medulla,** causing a rise of blood pressure, then a paralysis of the central nervous system, especially of the medulla and lower part of the cord. The animal injected shows in the beginning a rise of blood pressure succeeded by a fall and *arrest of respiration.* If the dose has not been so large it exhibits paralysis of the hind limbs and if it survives for a few days, profuse bronchial secretion is also observed. Death takes place from failure of respiration.

There is an insignificant **excretion** of silver by the gastro-intestinal tract, but none by the kidneys. No symptoms of renal irritation ever arise when silver is given internally to man or lower animals for very long periods of time.

GOLD also forms a compound with albumin which is violet and easily soluble in an excess of albumen; therefore it acts as a more powerful and deeper caustic than silver.

Given either subcutaneously or by the mouth, it produces nausea, vomiting, diarrhœa and pain along the intestinal tract. Ulcers are often found in the stomach and intestines. The kidneys are much irritated. With sufficient quantity, gold kills by paralysis of the central nervous system.

PLATINUM has an action closely resembling that of gold, but more powerful.

OSMIUM in the form of osmic acid is reduced by the tissues like silver and gold and causes a deposit of black pigment. When absorbed in sufficient quantities, it may cause irritation of the kidneys.

SUMMARY OF ACTION OF SILVER.—*Local astringent, antiseptic and superficial caustic. Internally absorbed very slowly and with small doses over a long period of time causes no other symptoms except "argyria," a deposit of the metal or one of its organic compounds in the connective tissue of different organs. With large internal doses symptoms of gastro-enteritis. Injected subcutaneously or intravenously as a double salt, first stimulation, followed by paralysis of the central nervous system.*

THERAPEUTIC APPLICATION.—**Silver nitrate** is used in the solid form or in concentrated solutions as a *caustic* to burn off warts, exuberant granulations and to clean badly healing ulcers. It is employed in dilute solutions as an *astringent* and *antiseptic* over the mucous membranes of the eye, nose, throat, vagina, urethra, rectum and colon in *gonorrhœal ophthalmia*, *urethritis* and *vaginitis* in *ulcerative colitis* and *prostatitis*, also as a preventive to eye inflammation in the newborn (Credé's method). It is sometimes used internally for *ulcers of the stomach* and intestines.

Organic preparations of silver as **protargol, argyrol, itrol,** and **argonin** have of late been used considerably as antiseptics instead of the nitrate. They are much less irritant, but also much less astringent and antiseptic.

Gold and **platinum** have been used in the treatment of syphilis, alcoholism, hysteria and epilepsy, but without any rational foundation, and also without good results.

MATERIA MEDICA.

Argenti Nitras (U.S.P., B.P.), colorless, transparent crystals, becoming greyish on exposure to the light or in the presence of organic material. It has a bitter, caustic, strongly metallic taste, soluble in 0.6 of a part of water, and in 26 parts of alcohol. Used as injection in the urethra in a $\frac{1}{10}$ to ½ per cent. solution. Applied to the eyes of the newborn in 2 per cent. solution, and in the colon in not more than $\frac{1}{10}$ per cent. **Dose:**—Br. ($\frac{1}{6}$–½ grain). Average (U.S.P.), **0.01 G.**

Argenti Nitras Fusus (U.S.P.), or lunar caustic, consists of fused silver nitrate and silver chloride. Used as a caustic.

Argenti Nitras Dilutus (U.S.P.), Argenti Nitras Mitigatus (B.P.), or mitigated caustic, consists of sticks containing 30 per cent. silver nitrate and 60 per cent. potassium nitrate. Also used as caustic.

The following organic preparations of silver are often used as substitutes for silver nitrate because they are less irritating.

Argentamine, solution of silver phosphate and ethylendiamine.
Argonin, compound of silver and casein.
Actol, lactate of silver.
Itrol, citrate of silver.
Argyrol, Largin and **Protargol,** all albuminates of silver.
All these are used in the same way of silver nitrate, but in considerably greater strength.

Auri et Sodii Chloridum (U.S.P.), yellow, deliquescent crystals, very soluble in water, with a metallic burning taste. **Dose:**—0.001 to 0.005 G.

GROUP OF IRON.

IRON is one of the most important constituents of living organisms and its presence is even more diffused than that of "salt," for it is found in the tissues of all animals and plants. In the former, the larger part is combined with hæmoglobin in the red blood corpuscles, yet quite a significant portion is present in the liver in the form of an acid albuminate. Every tissue, even the bloodless cornea, contains iron. In the plants this important metal plays often as important a rôle as in animals. At other times, plants may live without it, but have no chloropyl and their development is stunted.

Iron forms insoluble precipitates with albumins and, therefore, acts as an **astringent.** In strong solutions, it is an irritant and then a caustic on account of its affinity for the albumin of the living cells; for the same reason it is an **antiseptic.** The precipitate with proteids being insoluble, its effect is only superficial and not deeply penetrating like that of mercury. It also hastens the coagulation of blood and tends to arrest hemorrhage. The local action of iron is best seen with the inorganic forms as the organic have little or no direct effect.

Given in large quantities by the mouth in the form of one of its soluble inorganic salts, iron produces simply local corrosive poisoning exactly like the majority of other metals, with **symptoms** of pain in the stomach, nausea, vomiting, purging, both of which may be bloody, small pulse and even fatal collapse.

Injected into the circulation in the form of easily dissociable double salts, it causes its ion-action which consists of **gastro-intestinal** irritation, nausea, vomiting and diarrhœa which may

be bloody, congestion and even hemorrhage in the intestines, also great fall of blood pressure, paralysis of the **central nervous system** and death which takes place after 0.06 G. per kilo of body weight. The **heart** is not much weakened. In acute poisoning the **kidneys** are almost unaffected because the drug is excreted only in small quantities (about 2–3 per cent.) by these organs; but when small doses are given subcutaneously over a long period of time marked renal inflammation appears. The gastro-intestinal symptoms are due to the almost exclusive excretion of iron by this channel.

Administered by the mouth in small quantities over a period of time, iron is **absorbed** mainly by the duodenum and jejunum. It is carried to the spleen and liver and is temporarily stored as hepatic ferratin (iron albuminate) in the latter organ. It is there utilized to supply more iron to **red corpuscles,** and ultimately **excreted** by the intestines, especially the cœcum and large intestines. The quantity of iron normally excreted by the urine is not noticeably increased by its internal administration, and therefore when taken internally has no influence on the kidneys. The former view, that it acts as a diuretic, may be discarded. *The quantity absorbed from the intestinal tract is much greater when there is a deficiency of iron in the system.* Both the organic and inorganic salts of iron are absorbed and undergo the same fate, yet the former enter the circulation more easily and this is especially true of ferratin. The inorganic are probably transformed to albuminates before or during their absorption. The black stools after the administration of chalybeates result from the presence of the unabsorbed iron in the form of an oxide and sulphide. After the prolonged use of ferruginous preparations the teeth turn dark due to a precipitate of a sulphide by the sulphuretted hydrogen in the breath.

MANGANESE is found in traces in the organism yet no very important rôle has been discovered for it. In large doses of soluble salts, it causes gastro-enteritis just like iron and other metals. It is absorbed only in minute amounts from the intestinal tract, therefore, possesses no constitutional action except

after hypodermic and intravenous injections. Under these conditions it causes in large doses epileptiform convulsions, nausea, vomiting, diarrhœa, somnolence, collapse and death due to failure of respiration.

NICKEL and **COBALT** act upon the central nervous system, stomach and intestines very much like iron but unlike the latter they have no influence upon the hæmoglobin. No chronic poisoning is known even though a certain amount may be dissolved in the food by cooking acid elements in nickel pans.

SUMMARY OF GROUP ACTION.—*Iron is essential to the life of animal organism and after internal administration of both organic and inorganic preparations, it replaces the deficiency of this metal. Absorbed by the duodenum and jejunum. Excreted chiefly by the cæcum and large intestines. Very toxic ionic action when injected intravenously consisting of great depression of the central nervous system, especially well-marked fall of blood pressure due to vasomotor paralysis and respiratory failure. Symptoms of intestinal irritation also present from the excretion of iron by the intestines.*

THERAPEUTIC APPLICATION.—Both **Iron sulphate** and **chloride,** are used in solution locally as *astringent* and *antiseptic* washes or as injections to inflamed mucous membranes as those of the urethra and vagina. They are also employed as *styptics* to stop hemorrhage of wounds of the skin and of the mucous membranes of the nose, mouth, vagina, uterus, etc.

The chief use of iron is to increase the hæmoglobin in *anemic conditions*. Its most favorable field is in *chlorosis* and in this affection sometimes marvelous results are observed. One great drawback in the administration of iron internally is the constipation which it produces, because of its astringent action. This, however, can be overcome by the use of laxatives, or by employing the **organic preparations** which have but little astringent action.

MATERIA MEDICA.

Ferri Sulphas (U.S.P., B.P.), green vitriol, bluish-green crystals, soluble in 1.8 parts of water, insoluble in alcohol. **Dose:**—0.03 to 0.3 G. Br. (1–5 grains). Average (U.S.P.), **0.2 G.**

Pilulæ Ferri Carbonatis (U.S.P.), Pilulæ Ferri (B.P.), or Blaud's Pills, containing 0.16 of ferrous sulphate. **Dose:**—1 or 2 pills.

Ferri Chloridum (U.S.P.), orange yellow, deliquescent crystalline pieces, having a faint odor of hydrochloric acid. Soluble in water, alcohol and ether.

Liquor Ferri Chloridi (U.S.P.) contains 38 per cent. of ferric chloride. **Dose:**—0.1 to 0.5 c.c. Average (U.S.P.), **0.1 c.c.**

Tinctura Ferri Chloridi (U.S.P.) contains 25 per cent. of liquor ferri chloridi. **Dose:**—0.5 to 2.0 c.c. Average (U.S.P.), **0.5 c.c.**

Tinctura Ferri Perchloridi (B.P.). **Dose:**—(5–15 ♏).

Ferri Citras (U.S.P.), thin, transparent, garnet-red scales, odorless, having an acid reaction. Very soluble in water, insoluble in alcohol. **Dose:**—0.1 to 0.5 G. Average (U.S.P.), **0.25 G.**

Triferrinum is a ferric nucleate containing 22% of iron, 9% nitrogen and 2.5% phosphorus in organic combination. It is composed of a brownish, tasteless powder soluble in weak alkalies but not in weak HCl. It is by far the best of the organic preparations of iron on the market and contains one of the highest percentages of iron. **Dose:**—0.3–0.5 G.

Ferratin, a chocolate brown powder, composed of an albuminate of iron, insoluble in water, but slightly soluble in alcohol. It contains 6% iron. **Dose:**—0.5 to 1.0 G.

Ferri Oxidum Hydratum cum Magnesia (U.S.P.), or the antidote of arsenic, kept in two separate bottles; in one the hydrate of iron, in the other the magnesia, to be mixed before using. **Dose:**—Ad libitum.

There are on the market a considerable number of practically worthless organic iron preparations which contain from a fraction to a little over one per cent. iron, and in the doses recommended, their effect would be no greater than that of some of the ordinary food stuffs.

GROUP OF ARSENIC AND ANTIMONY.

ARSENIC has been of tremendous toxicological interest since the sixteenth century. It was used at that time in the form of the celebrated Aqua Tofana for homicidal purposes, and until the present, it has been the most celebrated poison in cases of suicide, homicide and accidental poisoning. Nevertheless, it was recently found to be normally present in minute traces in many living organisms including man. Certain of its actions resemble those of phosphorus with which it is chemically classed, yet there is a striking difference in the two, as phosphorus acts in the organism as the element, while arsenic exerts its effects by the dissociated ions of arsenious oxide, and those preparations which cannot be ionized into arsenious oxide do not have the characteristic action; thus arsenuretted hydrogen which cannot be oxidized in the system has an entirely different effect. The arsenic oxide

and its salts are much weaker but cause the same changes because they are probably transformed in the body to arsenites.

Cacodylates, organic compounds of arsenic, which are decomposed with difficulty, have at first an entirely different action, but later, as they become slowly transformed, they show in a lesser degree the characteristic poisoning.

When **ARSENIOUS ACID** is applied to the skin for a considerable length of time, it produces redness, vesicles and pustules, and if the tissue be denuded or if it be applied to a **mucous membrane,** it penetrates deeply and produces deep-seated necrosis. This action is not due to a coagulation of the albumen, as it forms no albuminous compounds outside of the body. But it is the result of a selective action on living protoplasm which arsenic possesses in a more marked degree than any other of the metals. By virtue of this property it is an irritant and caustic.

It has also a certain amount of **antiseptic action,** but much less marked than mercury. Even in great dilution it stops the growth of many higher plants and algæ. It possesses but slight action on the fungi and does not interfere with the activity of **unorganized ferments,** as pepsin, pancreatin, myrosin and emulsin.

Given by the mouth or injected subcutaneously, a large dose of arsenic produces in a short time **symptoms of poisoning** which consist of a burning sensation in the œsophagus, stomach and intestines, violent griping pain, vomiting, diarrhœic movements which may resemble the "rice water stools" of cholera, and may contain blood, flakes and pseudomembranes. The skin is blanched, the respiration weak and superficial, the pulse almost imperceptible. Great weakness develops and the patient becomes comatose; sometimes delirium and convulsions occur and he dies in from about five to twenty hours. When large doses are readily absorbed, the gastro-intestinal symptoms may be entirely omitted and collapse with coma and death may take place at the very beginning.

If less arsenic is taken or if the absorption is slow, the *gastro-intestinal symptoms* are very marked and after great vomiting,

diarrhœa and excruciating pain in the abdomen, death occurs in a few days or a week's time. In such cases skin eruptions, jaundice and enlargement of the liver may be present. The urine is scanty and contains albumin, casts, much ammonia and lactic acid, and the urea is diminished.

Following one large dose, if the subject lives long enough, or more commonly following the ingestion of repeated small quantities, a series of **chronic symptoms** arise. These consist of loss of appetite, nausea, vomiting, sometimes diarrhœa, discomfort and tenderness in the stomach and bowels and enlargement of the liver, inflammation of the respiratory passages and eyes, giving rise to bronchitis, laryngitis, coryza and conjunctivitis, disturbances of the skin resulting in eruptions and pigmentations and œdema, especially puffiness about the eyes, inflammation of the peripheral, sensory and motor nerves resulting in numbness, perverted sensations, shooting pains, paralysis of limbs, especially of the extensor functions, with ataxic gait, atrophy of muscles, psychical depression, sometimes idiotic condition and epilepsy, general cachexia with albuminuria, emaciation and sometimes death.

In acute arsenical poisoning, *death takes place on account of the paralysis of the* **blood vessels of the splanchnic area** which results in intense congestion of the intestinal organs and in a serious or fatal fall of blood pressure. The action is quite specific on the intestinal distribution of blood vessels, for those in other parts of the body do not suffer in the same degree. The effect is produced at first through the vasomotor centre and the splanchnic ganglia, but later the walls of the vessels themselves are affected. Not only is there a tremendous dilatation of the latter, but their *permeability is increased* so that they allow more easily the passage of fluids, and this fact explains the copious rice-water discharges. The increase in permeability in other vessels probably accounts for the œdema noticed in chronic arsenic poisoning.

The **nervous symptoms** of depression, the interference with respiration and the gastro-intestinal disturbances can all be explained by this intestinal congestion, attended by a great fall

of blood pressure. In warm-blooded animals, the nervous system is practically unaffected because death takes place too soon from fall of blood pressure. In frogs, descending paralysis occurs and the **heart** is weakened and stopped in diastole. The depression of the cardiac muscle is present, but is not so obvious in warm-blooded animals.

In the doses required to produce fatal acute poisoning, outside of the softening of the superficial layer of the epithelium, no real corrosion of the intestinal tract is seen, but only great congestion and even hemorrhages and also cloudy swelling and fatty degeneration of the cells. This **fatty degeneration** is best seen in chronic arsenic poisoning and involves besides the intestines, the heart, kidneys, liver, spleen and glands. It is probably the result of decreased oxidation, as is likewise the diminution of urea with the increase of ammonia and lactic acid in the urine.

When very minute doses of arsenic are given over a long period of time an increase in **weight,** in adipose tissue, in red blood corpuscles and hæmoglobin occurs. The augmented weight is probably due to the decreased burning up of food material which is more rapidly absorbed on account of a mild congestion of the intestines. The increase in the red corpuscles is probably due partly to the improvement of nutrition and partly to congestion and stimulation of the bone marrow. Not only the bone marrow may be stimulated, but the entire bone may grow larger and stronger.

As was previously mentioned, if doses eliciting poisonous symptoms are administered, the reverse effect takes place, i. e., decrease in body weight and in red blood corpuscles and hæmoglobin.

In the Tyrol and Syria the peasants take arsenic in large doses regularly without any apparent ill effects. They claim that it improves their general health and they undoubtedly live to old age. This is possibly explained by the fact that arsenic, being a normal constituent of the body, by gradually increasing the dose they gain high **tolerance.** The fact that arsenic miners in some other districts become badly poisoned, is apparently quite inconsistent. Yet they undoubtedly are

exposed to too large doses from the beginning so that before immunity occurs, they fall prey to the poisoning which is intensified by the bad hygienic surroundings attended by working in mines. An ingenious explanation for tolerance has lately been adduced by Cloetta. He believes that the intestinal mucosa gradually loses the power of absorbing arsenic after repeated small doses and that in this fact lies the explanation of the ability of arsenic eaters to take several times the fatal dose.

Symptoms of chronic poisoning may arise from the use of arsenic locally as a caustic, when too large doses are given in therapeutics, or from its accidental presence in food stuffs, clothing or wall paper. Whether symptoms are elicited or not, depends enormously upon the individual susceptibility. Of several persons exposed to the same amount of arsenic, usually only a certain percentage are affected while the other are not. Usually the train of symptoms differs in different cases, for instance individuals suffering from medicinal overdose usually show at first dyspepsia, puffiness of the lids and irritation of the eyes and nose and albuminuria; those poisoned from clothing frequently exhibit at the beginning skin eruptions, while workmen with arsenic in factories or mines are apt to suffer in the beginning from severe respiratory inflammation besides skin eruptions.

Arsenic is **excreted** mainly by the kidneys, but in small part by the skin, respiratory tract and bowel. It is found in the milk of nursing women. It is probable that the symptoms of irritation seen in the excretory organs in chronic poisoning are due to its passage through them.

The **temperature** may be elevated in arsenical poisoning from the inflammation of the intestinal tract, but when the symptoms of collapse are present it is usually subnormal.

ORGANIC ARSENIC PREPARATIONS.

For many years *sodium cacodylate* has been used in medicine to a small extent as a substitute for the simpler arsenic compounds, because it is much less toxic than the latter. The reason for this

lesser toxicity is due to the fact that cacodylates are only very slowly decomposed in the body with the formation of free arsenic. The amount of free arsenic liberated being so minute, it was found that cacodylates possessed very little arsenic action and were used less and less.

Ehrlich's work with the triphenyl-methane and benzidin dyes, and with a large group of synthetic arsenic compounds with the object of finding antiseptic agents which would kill pathological micro-organisms in the body and blood of animals and human beings, without proving toxic to the host, has given new interest in organic arsenical compounds.

One of the earliest of these substances which did prove successful in sterilizing the blood of some animals from trypanosomes was **atoxyl** or sodium arsenylate. At first great hopes were manifested in this substance, because it was much less toxic than arsenic and did have in some cases this marked sterilizing effect. It was recommended and used in trypanosomatous diseases, as dourine, tsetse, mal de caderas, etc. It was also used in syphilis. The action seemed to be due either to the molecule of the whole or to some partial decomposition product, but not to simple arsenic. The results, which seemed brilliant in a few cases, were very disappointing in others. The explanation of this soon appeared, when it was found that the *micro-organisms themselves easily acquired an immunity towards the drug* when repeated doses were given. Except in a few conditions in experimental animals, it was found impossible to give a single dose sufficiently large to produce the desired effect without harming the host. Further, it was soon discovered that atoxyl, though less acutely toxic, possessed far more frequent and severe **untoward effects** than arsenic itself. Among these symptoms were *dizziness, headache, fever, gastro-intestinal disturbances, as nausea, vomiting, diarrhœa and colic, nephritis and paralysis of nerves, giving rise to permanent paralysis of limbs, of the sphincters of the rectum and bladder, and of the optic nerve, resulting in partial or complete blindness.* Experimental works upon animals have shown, after small doses, destructive processes in the optic nerve and retina

and in the cord. These effects are probably produced, not by the ionized arsenic, but by the compound as a whole.

With the hope of overcoming all these untoward symptoms and also of obtaining a much more active drug, Ehrlich made the acetyl derivative which he called **arsacetin.** This compound had a history almost similar to the preceding, so that its use was soon dropped as a complete sterilizing agent in the blood. Nevertheless, it and others of these compounds were found to have far *greater antiseptic action if combined with other substances, as antimonial and mercury salts, than the sum-total of the action of each separately.* For this reason atoxyl and arsacetin have been employed combined with mercury in the treatment of syphilis with some degree of success.

Not discouraged by these two failures, Ehrlich set to work again, still more arduously, and after having synthetized and tested out 606 new arsenical compounds, he found in the one bearing that number, dioxydiamidoarsenobenzol, which was named **salvarsan,** properties of blood sterilization heretofore unequaled in any of the preceding ones in the series. This disinfectant action was particularly well marked towards the treponema pallida of syphilis. It is not highly toxic, for one gram has been given to man in a single dose without serious results. It has been calculated from the average monkey dose, that a human being might be given 5 to 6 grams at one injection without fatal results, but the actual test has not yet been made.

At first it was claimed that a single injection was completely curative as far as removing the presence of all the symptoms of syphilis, including the Wasserman and the Noguchi reactions. Within a few months after the first appearance of this much-lauded substance, innumerable articles began to appear and still continue to do so, denying the curative effect of a single dose in either secondary or tertiary syphilis. Concerning the primary stage, opinions are divided, but it seems highly probable that many cases may be cured.

Besides the reports denying a wonderful curative power to salvarsan, hordes of case-records have been published showing

untoward effects and sudden death resulting from one to three injections of salvarsan. One of the disagreeable untoward effects has been the great local reaction with even gangrene and exquisite pain at the site of injection by the subcutaneous or intramuscular method. These results have led to the use of the intravenous method. Such symptoms as headache, vomiting and fever are not uncommon. Cases of hemiplegia and other paralyses followed the use of salvarsan.

The type of **fatal cases** runs about as follows: one to two days after the injection, the patient experiences violent headaches, generalized pain in all the limbs, sometimes paralyses, nausea and vomiting, convulsions and death in coma. Such deaths have occurred in several young subjects twenty odd years old.

The action of **ARSENURETTED HYDROGEN** is quite different. This compound is also very poisonous, producing destruction of the **red corpuscles,** methæmoglobinuria, cyanosis, headache, vomiting, garlicky odor in the breath, and death due to paralysis of the heart and sometimes to œdema of the lungs, but it does not have the characteristic effects of the ions of arsenious oxide.

ANTIMONIAL compounds have an action almost identical to that of arsenic. They differ because they are much more difficultly absorbed and have a greater local irritant action. The main symptoms are intense nausea, **vomiting,** diarrhœa and collapse. The vomiting is so rapid and intense that most of the antimony is removed by emesis, and, therefore, fatal results are much less frequent than with arsenic.

The small quantities absorbed after internal administration are excreted in part by the respiratory tract so that there is irritation of these parts. This action plus the feeling of nausea tends to increase the bronchial secretion. Antimony is also excreted by the urine and feces. Chronic poisoning rarely occurs on account of the poor absorption.

Like arsenic, antimony was also used to make organic compounds which might have *sterilizing influence in the blood* of the living. Among these was one analogous to atoxyl, paraamino-

phenylstibinic acid, which was found to be very active in lower animals affected by trypanosomiasis. It was also recommended and used, to a certain extent, in the treatment of sleeping sickness in human beings. It produces, unfortunately, marked untoward effects, among which is irritation of the kidneys. More recently, Abel and Rowntree have experimented with compounds of antimony with thioglycolic acid. They have obtained most encouraging results in experimental animals with sodium antimony thioglycollate and the triamide of antimony, thioglycolic acid, and warmly recommend that these compounds should be tried in human beings for the sleeping sickness.

SUMMARY OF GROUP ACTION.—*Destructive action to life of cells but no influence upon dead proteid, therefore, irritant and caustic action different from that of all other metals. Taken internally in large doses, paralysis of vessels of splanchnic area which causes a great fall of blood pressure, choleric discharges from the bowels, collapse and death. The chronic poisoning is due to the irritation and degeneration of the central nervous system, peripheral nerves, skin, kidneys and gastro-intestinal tract and is accompanied by serious disturbances of metabolism. Very minute doses insufficient to produce poisonous symptoms improve the general metabolism.*

THERAPEUTIC APPLICATION.—**Arsenic** was used locally as a *caustic* to burn off new growths. This use has been laid aside on account of the occasional occurrence of poisoning from absorption. It is applied in dentistry to kill the nerves of teeth.

Internally it is employed for its effect on metabolism to improve almost all conditions of *malnutrition*, in *anæmia* to increase the red blood corpuscles and also in long-standing *malaria*. Here its good effects may be due either to improvement of metabolism and of the anæmia or to a special action against the malarial parasite.

In *lymphoma*, where it is sometimes used with good effect, its action may possibly be due to the production of a retrograde metamorphosis in the lymph glands.

Arsenical preparations have an important field in the treatment of certain *skin diseases*, especially *psoriasis*. They may produce

beneficial influences in these conditions, either by improving the general metabolism or the special metabolism of the skin. The latter view is rather supported by the fact that arsenic is normally present in appreciable quantities in the corium.

Salvarsan, and to a less extent, atoxyl and arsacetin are used in the *treatment of syphilis*. Salvarsan, which is much less poisonous and much more active has to a great extent replaced the other two. As has been said in describing its pharmacology, it does not have the absolutely marvelous curative powers which were attributed to it when first discovered. Nevertheless, it often benefits cases which are not affected by mercury, and when given in conjunction with the mercurial treatment, it greatly diminishes the length of the treatment, so that instead of waiting three to four years a patient may be cured in from a few months to a year. Salvarsan is said also to be active in relapsing fever, in frambesia, in yaws, in filaria and in tertian malaria. It has not been found active in the quartan nor in the estivo-autumnal malaria, nor in leprosy.

The **treatment of acute arsenical poisoning** consists of the administration of freshly precipitated ferric hydrate or ferric hydrate and magnesia, which form an insoluble compound with arsenic. An emetic should be given at once, or the stomach should be washed and a cathartic administered, because this insoluble compound may be again decomposed if left in the alimentary canal.

Chronic arsenical poisoning which comes from contaminated articles of food and sometimes clothes and wall-papers containing arsenic, is treated by removing the cause, improving hygienic conditions and meeting the different symptoms as they arise.

Antimonial preparations are used almost exclusively as *emetics* and expectorants. Nowadays, they are employed even for these purposes much less than formerly, because there are other less poisonous expectorants and emetics. Some of the organic preparations of antimony are used against the various trypanosomatous diseases.

MATERIA MEDICA.

Arseni Trioxidi (U.S.P.), Acidum Arseniosum (B.P.), heavy, opaque, white powder, or irregular masses, either amorphous or crystalline, soluble in 80 parts of cold water and 15 parts of hot water. **Dose:**—Br. ($\frac{1}{60}$–$\frac{1}{12}$ grain). Average (U.S.P.), **0.002 G.**

Liquor Potassii Arsenitis (U.S.P.), Liquor Arsenicalis (B.P.), 1 per cent. solution of potassium arsenite. **Dose:**—0.1 to 0.5 c.c. Br. (1–8 ♏). Average (U.S.P.), **0.2 c.c.**

Antimonii et Potassii Tartras (U.S.P.), Antimonium Tartratum (B.P.), or tartar emetic, colorless, transparent crystals which become opaque in the air and have a sweet metallic taste. Soluble in 17 parts of water, insoluble in alcohol. **Dose:**—0.1 to 0.2 G. Br. emetic (½–2 grains). Average (U.S.P.), emetic **0.3 G.**; expectorant **0.005 G.**

Antimonium Sulphuratum (B.P.), or Kermes mineral. A reddish white powder, insoluble in water and alcohol. **Dose:**—0.01 to 0.05 G. Br. (1–5 grains).

Salvarsan (dioxydiamidoarsenobenzol) is a light yellow powder kept in sealed glass capsules free from air, but containing the vapors of methyl alcohol to preserve it from oxidation. It is an acid body combining readily with alkalies. It is freely soluble in water, but is precipitated out by alkalies in small and redissolved by larger amounts. **Dose:**—0.3–1.0 G.

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